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TOXICITY TESTING OF CHEMICALS

HEARING

BEFORE THE

SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT

OF THE

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS UNITED STATES SENATE

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TOXICITY TESTING OF CHEMICALS

TUESDAY, APRIL 10, 1984

U.S. SENATE, COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS, SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT,

Washington, D.C.

The subcommittee met at 3:14 p.m. in room SD-406, Dirksen Senate Office Building, Hon. Dave Durenberger, chairman of the subcommittee, presiding.

Present: Senator Durenberger.

OPENING STATEMENT OF HON. DAVE DURENBERGER, U.S. SENATOR FROM THE STATE OF MINNESOTA

Senator DURENBERGER. The hearing will come to order.

I apologize to the witnesses and others for being late. I am a member of the Senate Select Committee on Intelligence, and we have just been spending time since prior to 2 o'clock on a subject dealing with Nicaragua which I am sure you are aware of and which there is going to be a vote on in the Senate at 5:30. I regret that other members of this committee weren't able to be here in my absence.

Today's hearing is about testing chemicals for their possible toxic effects. The question before the subcommittee is: How much do we know—or more important—how much do we not know—about the toxic potential of the manmade chemicals we encounter in our daily lives?

We live today in a world dominated by manmade chemicals. U.S. production of chemicals has increased twelvefold since the end of World War II. Synthetic organic chemical production has nearly doubled just in the last 15 years. EPA listed about 55,000 industrial and consumer chemicals in commerce in 1977 and currently is reviewing about 1,000 new ones each year. Just the top 50 chemicals alone amount to around 500 billion pounds of production annually. That is close to a ton of chemicals for every person in this country, each year. Add to that about 3,300 pesticide chemicals, 3,400 cosmetics, 1,800 drugs, and 8,600 food additives, and you begin to get a picture of the task we face as a society in assuring that we are not subjecting ourselves, our children, or the environment to unacceptable risk.

However, according to a recent prediction by Business Week, the chemical industry can expect $220 billion in sales in 1984, a 15-percent increase over 1983, so it seems reasonable to assume that the industry can afford to test these products adequately.

It was the recognized need to identify and control these risks that prompted the plethora of chemical regulation laws that now exist at the Federal and State level. But almost no one would argue that these laws have been as effective as they should have been. Striking failures of the regulatory process have been documented—the recent example of EDB comes to mind—and we find ourselves waiting to see which chemical will be the next one to make headlines.

As I have participated in hearing after hearing and read many articles on toxic substances and hazardous chemical issues, I have realized that one message comes through again and again. That message is that we just do not know enough about most of the chemical substances to which we are exposed throughout our lives to know what risks we are taking. For example, the head of the drinking water program at the Environmental Protection Agency told us that he does not have enough toxicity data about the many common organic contaminants of drinking water to set recommended maximum contaminant levels for them. The same lack of information has hindered the Superfund program's ability to set cleanup standards for hazardous waste dumpsites. EPA has testified that it will take until the late 1990's to get the necessary toxicity data and to review already registered pesticides.

At this hearing we will hear about the first attempt of which I am aware to systematically measure the extent of our ignorance. Only after we understand the nature and scope of the problem can we find solutions. We need to know how large and how serious is the toxicity data gap. We need to know whether the capacity exists in toxicology laboratories to accelerate the pace of testing. We need to know whether important toxicity data is being withheld from the medical community, regulatory agencies, and the public. Then we must find a way to effectively attack the toxicity data gap.

I will now call the first panel, Dr. John Bailar, Dr. Doull, Dr. Emil Pfitzer, and Dr. Liverman to the witness table.

STATEMENT OF DR. JOHN C. BAILAR, LECTURER IN BIOSTATISTICS, HARVARD SCHOOL OF PUBLIC HEALTH

Senator DURENBERGER. All your statements will be made part of the record. I understand that the first three named witnesses will be testifying, in part, on behalf of the research of the National Academy of Sciences and that they may also have some personal professional statement to add at the conclusion of their testimony. So we will begin with Dr. Bailar.

I want to be sure that we include in the record the document entitled "Toxicity Testing, Strategies To Determine Needs and Priorities." [See p. 39.]

Dr. Bailar.

Dr. BAILAR. Thank you.

With your permission, the three of us will each give short statements, and then return the discussion to me for an even briefer joint statement.

Senator DURENBERGER. You have that permission.

Dr. BAILAR. In 1980, the national toxicology program contracted with the National Academy of Sciences for a study with two main

charges. Doctors Doull, Pfitzer, and I worked on one of these, which was to characterize unmet needs for testing the toxicity of substances with known or expected human exposure. More than 5 million chemical compounds have been described in the scientific literature, and the list continues to grow rapidly, but most of these compounds are made only in laboratory quantities or for other reasons could have little or no effect on human health and survival.

Also, resources available to the committee did not permit a search of the whole 5 million substances to determine which ones might be of public health interest. We therefore focused attention on existing lists of chemicals that had various characteristics which, summarized, are that they be made in high volume, that they have known substantial biologic effects, or that they have prolonged, direct, substantial human exposure. We felt that such chemicals would be the ones of primary concern.

In the end, we worked with five lists: One from the Environmental Protection Agency of registered active ingredents of pesticides and inert ingredients approved for use in pesticide production; second, a list of cosmetic ingredients; third, the FDA list of drugs and excipients in drug formulations; fourth, segments of the FDA chemical dictionary, those segments containing approved food additives, and last was EPA's list of what are known as chemicals in commerce, generally those chemicals produced in quantities of at least 1,000 pounds per year by at least one manufacturer.

The list of chemicals in commerce was then subdivided into three parts on the basis of what we have learned about the volume of production.

There were, altogether, close to 66,000 entries on these lists representing 53,000 separate substances after we removed the duplicates. Items on these lists were first studied for the simple presence or absence of several critical kinds of data, without regard to whether the data were good or bad. This is evaluation in its simplest and crudest form: If someone reported that a study had been done, we counted it.

Those chemical substances that were found to have at least this minimal information on toxicity were eligible for inclusion in a second stage sample for such more detailed study.

Altogether, 675 substances were chosen for the initial sample, and 100 of these, spread over the total of 7 lists and sublists, were chosen for the second stage.

Drs. Pfitzer and Doull will describe what was learned from those samples. Before they do, I would like to mention several other things. First, we have good reason to believe that some information was filed in old records at both industry and Government but was not or could not be made available to us. Our approach to this matter was that if we could not see the data, others probably could not see the data either, so that the study was of no current value in assessing the hazard of the item on these various lists, all of high volume or high exposure or high biologic impact. In an operational sense, if we could not see the data, we assumed that the data effectively did not exist.

Also, there were some severe constraints on sample sizes, especially at the highly labor-intensive second stage of sampling. We found quite early that not more than 100 substances could be in-

cluded in the second stage, and we then faced a critical policy question. Should we try to learn a lot about one or two of these lists, or should we try to learn a little bit about each of the sublists. We chose the latter course, thinking it was better to learn a little about each of the major areas.

What, then, can be learned from this study, especially when the samples in the second stage are small and the statistical confidence limits are wide? One can, in fact, learn a great deal because of three critical features of the data. For one thing, the second stage findings tended to generally support and extend the rougher first stage findings. Both showed serious and widespread gaps in knowledge about the toxicity of chemicals that are common in our daily lives. When the first and second stages are considered together, conclusions seem to be solidly based.

The second general point is that findings from the separate parts of the second stage sample strongly reinforce each other. If one were to find something in a sample of just 10 or 15 compounds, one might tend to dismiss it, but that becomes harder to do when the same finding appears in a second sample of 15, and again in a third, and so forth. Each of the seven parts of the second stage sample, small as they were, showed serious gaps in toxicity knowledge available to protect the public.

Finally, even the very wide confidence limits in our results may have their uses. If we estimate, for example, that some critical test of drugs has been performed for something between 5 and 60 percent of drugs and their excipients, the person who thinks the figure should be close to 100 percent will not be satisfied. Again, we believe that these small samples do establish some critical gaps, big gaps, that should not be there.

Thank you.

STATEMENT OF EMIL A. PFITZER, DIRECTOR, TOXICOLOGY AND PATHOLOGY, HOFFMANN-LA ROCHE, INC.

Mr. PFITZER. Mr. Chairman, my name is Emil Pfitzer. I am director of the department of toxicology and pathology in the research division of Hoffmann-La Roche, Inc., Nutley, N.J. I served on the Committee on Toxicity Data Elements for the National Academy of Sciences' report on toxicity testing.

My presentation here is as a participant in this National Academy report, and I have been asked to discuss the quantitative nature of toxicity testing needs.

First, I wanted to make five important points about this report:

One, we believe the report provides a very sound scientific framework for assessing the need for toxicity testing;

Two, we found a significant need for more toxicity information;

Three, this document cannot be used to make judgments about the potential toxicity of the substances;

Four, we recognize that there are some limitations to our findings; and

Five, there is a need to establish priorities and allocate resources to perform the toxicity testing on those substances that need further testing.

I will elaborate briefly on these points. Regarding the first point about our scientific framework to assess toxicity testing, it may be well to define what we mean by toxicity testing. We mean studies to determine when a substance is safe and when it produces unwanted effects. This could depend upon the conditions of exposure in terms of: Concentration; duration; frequency; and whether a substance is swallowed, inhaled, injected or applied to the skin.

We agreed to study a select group of substances based on their potential for human exposure. Because of economic and time considerations, we limited our comprehensive review to 100 substances but made a limited review of 675 substances. It is important to emphasize that this sample is a representative cross-section and was not limited solely to substances of toxicological concern. For example, the sample of drugs and excipients contains ingredients such as gelatin, lactose, cottonseed oil, and peanut oil, for which there is less toxicological concern than the active ingredients of drug formulations.

We used two measuring sticks for our evaluation. One measuring stick was a list of the toxicity tests that would be required for substances intended for a specific use. For example, a drug limited to use for the eyes required a different set of toxicity tests than did a direct food additive. The other measuring stick consisted of state-of-the-art protocols on how to conduct each type of toxicity test.

We then reviewed all the available toxicological information for the 100 substances. Using our two measuring sticks, we documented on an item-by-item basis whether or not by today's standards all of the required tests for a specific intended use had been done and if they had been conducted following the recommended protocol.

In some cases, such as for gelatin, the committee also documented that no further tests were needed even when the full requirements of the two measuring sticks were not met. This determination was based upon collective scientific judgment and knowledge of human experience with the substance.

The second point was that the characterization of the need is presented in numerous tables in our report. The quantitative findings are best summarized in table 20 and figure 2. The process of deriving the summary is complicated, but I will try to explain it.

For each substance in the sample we looked at the toxicological information available, used the measuring sticks just defined to judge both the appropriateness of the test and the quality of the test, and then placed the substances in one of five health hazard assessment classifications.

These are: First, a complete health hazards assessment which was possible if enough information was available to know how to use the substances safely; second, a partial health hazard assessment which was possible when there was limited information about the substance to make a safety judgment; third, minimal toxicity information which was available as required for section into the sample and which varied with the categories of substance; fourth, some toxicity information which was less than that required for selection into the sample; and fifth, no toxicity information available, based only upon the limited search used for selection of the sample.

Using the findings for the pesticides and the inert ingredients of pesticides as an illustrative example, it is seen that there was an

estimate of sufficient toxicity testing information on 10 percent of the substances to make a complete health hazard assessment.

There was an estimate of an additional 24 percent of the substances in the sample for which it was possible to make a partial health hazard assessment, and an additional 2 percent with only minimal toxicity information available.

For the remaining substances which represent 64 percent of this category there was little to no information, and an assessment of health hazard was not possible with the information obtained from the limited search for sample selection. Each of these percentages is subject to an uncertainty expressed as 90 percent confidence limits.

Evidence further substantiating the need for more toxicity information is provided by looking at the estimated percentages of substances in each of the seven categories for which no toxicity information was available. This ranged from a high of 82 percent for some chemicals in commerce to a low of 25 percent for drugs and excipients used in drug formulations.

The third point—and perhaps the most significant conclusion from a public policy standpoint—is that these findings cannot be used to make any judgments about the potential toxicity of the substances. Our report makes judgments as to whether or not categories of substances had been adequately tested—but it does not address the nature of the toxic hazards that may be associated with the substance.

The fourth point is that while we believe that we have clearly established that a significant need for additional toxicity testing exists, we also are aware of the limitations to our quantitative estimates of need. Some of the limitations are handled by statistical techniques leading to the range of confidence limits for the estimates.

Another limitation is the lack of information about exposure to a given substance. It is possible that many of the substances have little likelihood of significant exposure that would affect health and may not need further testing. The dilemma is that information on exposure was not generally available.

Other limitations are inherent in the database used for the estimates. For example, it is certain that for some of the substances we did not have all existing data available to us. For the purpose of our calculations, as Dr. Bailar mentioned, if data were not available they did not exist. Obviously, additional data would improve the situation.

It is also important to recognize that the estimates in the report are for a universe of substances for which some toxicity data was collected 40 or more years ago, and such data reflected state-of-the-art expectations in those earlier times in contrast to the high level of activity today.

The fifth and final point is that there is a need to establish priorities and allocate resources to perform the toxicity testing on those substances that need further testing.

We believe that we have provided a sound scientific framework for assessing the need for toxicity testing; that we found a significant need for more toxicity information, but that the nature and

degree of the potential toxic hazard associated with the substances having inadequate testing cannot be determined from our report.

It is my opinion that it is very prudent that resources be allocated so that the national toxicology program can establish mechanisms and priorities to meet this need.

Thank you, Mr. Chairman.

Senator DURENBERGER. Thank you.

STATEMENT OF DR. JOHN DOULL, PROFESSOR OF PHARMACOLOGY AND TOXICOLOGY, UNIVERSITY OF KANSAS MEDICAL CENTER

Dr. DOULL. Senator, my name is John Doull. I am a professor of pharmacology and toxicology at the University of Kansas Medical Center in Kansas City. Like my colleagues, I appreciate the opportunity to appear before you to discuss the recent report of our committee on the current state of toxicity testing of chemicals in this country. As has been mentioned, the responsibility for selecting and testing chemicals, potentially toxic chemicals has been assigned to the national toxicology program which is a Federal Agency established in 1978 within the Department of Health and Human Services.

Three years ago, the NTP, through the National Institute of Environmental Health Sciences, requested the National Research Council of the National Academy of Sciences to conduct a study to characterize the toxicity testing needs for substances to which there is known or anticipated human exposure and to develop and validate uniformly applicable and wide-ranging criteria to set priorities for research on substances with potential adverse public health impact.

Our focus today, of course, is on the first of these tasks, the toxicity texting needs.

To carry out this task, our committee asked two questions: First, how much toxicity testing has been carried out on those chemicals in the various classes of agents which constitute the university of chemicals to which man is exposed; and second, how good is the testing that has been carried out with these chemicals?

Dr. Pfitzer has discussed the results of our committee findings in response to the first question, and I would like to summarize briefly our findings in response to the second question.

To evaluate the quality of the individual toxicity tests that have been performed on each of the various chemicals included in our study, our committee used a battery of reference protocol guidelines which, in most cases, were those of OECD or the Organization for Economic Cooperation and Development; the IRLG, or the Interagency Regulatory Liaison Group, and the National Research Council Protocols. For some tests in which there were no generally accepted current guidelines, such as neurobehavioral toxicity, our committee adopted a protocol based on the current state of the art in that area.

In this exercise, our intent was not to endorse any particular test or set of guidelines or protocol but rather to develop a yardstick, as Dr. Pfitzer has mentioned, which we could use in evaluating the toxicity data base for all of the candidate chemicals in our study.

We recognize that by using the most current protocols for these comparisons, older agents which were approved on the basis of previous protocols might be considered to have testing deficiencies.

Because of this, our committee used the second criteria to further evaluate the quality of the data in the toxicity data base for each of these compounds. For each toxicity test that failed to meet the reference protocol guidelines, the committee made a judgment as to whether the test results were adequate to make a health hazard assessment or whether the test needed to be repeated in order to make that decision.

Our committee evaluated a total of 664 tests which were carried out on 100 compounds in the subsample. When judged against the reference protocol guidelines, only 8 percent of these tests met this criteraa, although an additional 19 percent of the tests were judged by our committee to be adequate for making health hazard assessments.

In general, the acute toxicity tests satisfied the reference protocol requirements more frequently than did the chronic tests. Our committee identified our acute tests; acute oral, acute dermal, dermal irritation, and eye irritation in which 75 percent or more of the tests were judged to be of adequate quality. However, we found that only half of the carcinogenicity tests and less than a third of the reproductive tests were considered to be of acceptable quality. The most common cause of failure to meet reference standard protocols guidelines were too few animals per dose group, there were too few or improper dosage levels; there was absence of clinical or histopathologic observations.

We were fortunate to have on our committee a group of eminent toxicologists with long experience in evaluating this type of toxicity test information. It was only because of this availability of this experience that our committee was able to utilize toxicity testing data on compounds that had protocol deficiencies. In other words, we substituted scientific judgment for data in some cases to make the health hazard assessment.

We judged some of these deficiencies, for example, to be adequate on the basis that further tests would not be expected to alter the toxicologic conclusions for the compound or because the existing data on that compound was sufficient to evaluate its toxicity.

Within the various classes of chemicals, the toxicity tests were judged to be adequately performed more frequently with presicides, drugs, cosmetics, and food additives than the chemicals in commerce or the TSCA compounds. This finding, together with the finding that the chemicals in commerce have the smallest amount of information relevant to human exposure in the work place and in the general environment, was of particular concern to our committee.

We recommend, therefore, that in addition to the need for further testing, that a coordinated effort be made to collect information needed to assess potential human exposure in the workplace and in the general environment.

Thank you very much.

Senator DURENBERGER. Thank you very much.

Dr. BAILAR. May I return to the joint statement?

It is natural to ask, now, what can and should be done to reduce the significant gap in toxicity testing and to mitigate its effects while the gap is brought under control. Our committees did not address this question directly. As interested individual observers, however, we see several potentially useful steps. First is to supplement the data gathered by the NAS committees. Several extensions are needed: Larger samples; a better understanding of the nature and extent of data not available; targeted study of additional lists of substances of great concern; and a more detailed study of several specific technical issues.

Second, is to begin promptly to build a national base for an expanded, better targetted testing program. Many of the most qualified persons and facilities are already dedicated full time to this effort and cannot take on additional work. The most critical requirement is to learn how to produce more, and more relevant, information from whatever level of investment is available for toxicity testing. Thus, the first need is to expand the research base for developing new testing methods that are less resource-intensive as well as more informative about both safety and risks.

In addition, we see a need for substantial net additions of professional and technical personnel, toxicologists, statisticians, biochemists, laboratory animal technicians, and many others. Unused physical facilities and other resources should be surveyed and inventoried so that needs for new facilities can be accurately judged.

Third, is to make the problem more widely known to the scientific community, to legislators, to regulators, and to the public. There is reason for substantial concern, but little will happen unless the problem is generally recognized.

And fourth is to follow through with a more formal approach to setting priorities for toxicity testing. It will take many years to work off the backlog of needed testing, and it may never be possible to do all testing that seems desirable. Which substances should be tested first and which tests should be applied first? We may fall even further behind unless priorities of truly national scope are developed for use by a range of Government agencies, including State and local governments, affected industries, university scientists, and other interested parties. Without national priorities, it is likely that significant gaps will persist, scarce resources will be diverted, and the necessary broad effort will be delayed.

We regard this National Academy report as a first step in meeting a significant national problem, and we look forward to future actions by the national toxicology program and other public and private groups.

The three of us are grateful for this opportunity to bring this matter to the attention of the subcommittee. Thank you.

Senator DURENBERGER. Thank you very much.

STATEMENT OF JAMES L. LIVERMAN, VICE PRESIDENT, NATIONAL ASSOCIATION OF LIFE SCIENCE INDUSTRIES, INC.

Dr. LIVERMAN. Mr. Chairman, my name is James Liverman. I'm a vice-president of the National Association of Life Science Industries, a nonprofit trade association representing a number of inde-

pendent toxicology testing laboratories, often referred to as contract testing laboratories.

I am also a senior vice president and general manager of Litton Bionetics operations in Maryland in which we have some 88,000 square feet of animal testing facilities and the largest in vitro genetic toxicology testing laboratory in the business. Thus, I feel I have some reason to have knowledge about toxicity and toxicology testing.

We read with great interest the splendid report prepared for the National Academy of Sciences, and I am honored to appear on the panel with three members, three of its distinguished authors. You have heard the report summarized, and we basically agree that there are large number of chemicals existing in commerce and in man's environment that have not adequately been tested. Clearly, additional testing is indicated.

As has just been pointed out, there are three or four sharp questions that have to be asked resulting from this report: Does the Nation have the capacity to do additional testing? Does the right kind and the necessary level of technical expertise exist? If the commercial toxicology contract testing laboratories are to be involved, are they credible in the public eye? I would like to speak to each of these three points very briefly.

The FDA maintains a list of toxicity laboratories which are subject to inspection under its good laboratory practice regulations. That list comprises some 400 organizations. It should be noted, however, that the list encompasses government, university, nonprofit, product sponsor laboratories, and the independent toxicology testing laboratories, many of which are very small.

In 1981, another study entitled "Chemical Testing Industry Profile of Toxicological Testing" was completed for the EPA. This report estimated the number of independent contracting and captive in-house commercial toxicology laboratories at approximately 285. Of these, about 35 percent were independent and 65 percent were captives of the product industry or were university based. We estimate that of the so-called contract laboratories, approximately 20 of those, so 20 out of the 34 percent of 285 do about 85 to 90 percent of the commercial contract testing business. An important point, however, is that some of the remaining smaller laboratories are highly specialized in some areas and provide for that specialty area in the majority of the testing.

For a number of reasons which my panel member colleagues will fully appreciate, it is difficult to make a precise estimate of the available excess testing capacity since so much depends upon the end point being measured, the animal models being used, the route of exposure to the chemical and the nature of the chemical itself.

In addition to this spectrum of animal tests, there are an increasing number of in vitro tests that yield large amounts of information at low cost in a relatively short time. Few laboratories have the broad spectrum of competence to deal with all of these testing areas.

Despite this complexity, however, in toxicology testing, we estimate that at the present time there is physical capacity in the contract testing laboratories to increase, by at least 30 percent, toxicity testing. The reasons for this excess capacity derives, in part,

from the construction of facilities by the industry in the late 1970's in the anticipation of the testing to be required by a number of environmental acts passed by the Congress: FIFRA, the Federal Insecticide, Fungicide, and Rodenticide Act; the Toxic Substances Control Act; the Resource, Conservation and Recovery Act; the Federal Food, Drug and Cosmetic Act. These anticipated requirements never really fully eventuated, thus, there was left in the hands of the testing industry some considerable excess physical capacity.

The EPA study mentioned above states that 73 percent of the labs offered additional capacity, some of them, in fact, over half, having about 30 percent available. Remember, that study was done in 1981 before the full impact of the recent, we hope past, recession, which increased measurably, then, the physical capability to test and although precise excess current capacity would have to be determined by an update and a review of that study done in 1981, my guesstimate, which is different than an estimate, is that right now you would find between 30 and 50 percent excess testing capacity does exist in the laboratories.

At the same time that this excess capacity has become available, the toxicology test methods have become increasingly sophisticated and more complex.

Thus, one of the principal limiting factors to a deliberate expansion of the capacity to test is going to rest on the need for—which has been pointed out by the members of the National Academy of Sciences Committee—for more highly trained manpower and certainly, it depends upon a consistent level of funding.

Intimately interwoven with this question of capacity and confidence is the question of credibility. In NALSI we have taken several steps recently to strengthen public confidence in the business ethics practiced in our industry. NALSI prepared and its members have subscribed to a new strict code of ethics. We believe that with time, the remainder of the testing industry will follow NALSI's lead and also adopt this or a similar code. A copy of the code has been provided to the subcommittee staff along with a copy of a recently prepared brochure entitled "A Message to a Challenged Industry." NALSI has taken a further step in that its members have agreed to a program of outside, independent inspection and peer review of scientific skills, personnel, and facilities.

Following such a review, if successful, the laboratory then receives accreditation, thus making it known to the public and to the people who want testing done that the skills and the facilities which we claim to have as individual laboratories do, in fact, exist.

We have also endeavored to draw the attention of the public and the industry to increase their understanding of toxicity testing and to advance the design and management of the testing laboratories. We have made available to the subcommittee staff a copy of the proceedings of an international conference held about a year and a half ago by NALSI on "Toxicology Laboratory Design and Management for the Eighties and Beyond," which brought up to date the state of the art needed in physical facilities at that point in time for toxicology testing.

In summary, Mr. Chairman, I would like to say that we in the contract testing laboratory business have available considerable ca-

pacity, the capability and the desire to undertake the additional testing as required. The manpower issue is one that will be dealt with in time. I appreciate the opportunity to appear before the committee.

Senator DURENBERGER. Thank you very much, Doctor.

I thank you all for your statements, and those of you who participated in the study, I am grateful to you. I notice the results of the study got a few paragraphs in the New York Times relative to the discovery of EDB. What you have told us is almost negligible as far as the impact on the public is concerned, and yet for those of us who care about the nature of the problem which you were charged with undertaking, it was a very, very significant statement about the condition of this country.

One of the issues that always faces us when we undertake to solve a problem of this dimension is the issue of resources. The last witness has, at least in some part, addressed the issue of resources and talked about the present capacity, skills, and credibility in the area with which he is familiar. I wonder if I might ask that question of the first three witnesses in terms of the capacity, the skill, and the credibility of our toxicological resources in this country to handle the problem if we did some of the things that your statement said that we ought to do.

Dr. BAILAR. Our committees did not consider directly the question of how much expansion in testing capacity is needed. We think we have documented a need for a very substantial expansion, primarily in the areas of knowledge about how to do testing; that is, research on the testing process; and in the area of training of people who are qualified to do high quality testing.

We feel also that there should be the survey of facilities and other resources including personnel. At the conclusion of an adequate survey of that sort, I think one would be in a much better position to say how much expansion is needed. Clearly, there is a lot that is needed, but whether we are talking about twofold or fivefold, or tenfold, we can't say at this point.

Senator DURENBERGER. Just in your own individual opinions, how concerned should we be about the problems that you have pointed out to us? Obviously, you can look around this room and you don't see any Senators, you don't see any television cameras, you don't see a lot of attention focused on this particular hearing, but it doesn't mean that the people out there in America are not in some way concerned. How far should we lift the level of our concern about the results of your findings or is it something we ought to store away and pass out to the appropriate Federal agencies and ask them to read it and react? What should our next step be in a committee like this?

Dr. BAILAR. Senator, you ask how much concern? It is hard to put that on scale. I thought about this a little myself and would say on a rough verbal scale that it is certainly at the level of substantial concern, but it does not reach the stage where there is any call for panic. I think there is a serious problem. We ought to move expeditiously to begin solving it, but I don't see any need for widespread public distress about this factor.

Senator DURENBERGER. Let me ask the question and maybe the other gentlemen can react in a slightly different fashion. Do you

have a concern about a sense of direction? In other words, were we less concerned 5 years ago than we are today and you can see a building concern and do you feel better about the rising level of concern about the issue today than you might have 3 years ago when you started this study or 5 years ago?

What is your sense of the direction of the concern of this country in the areas you have undertaken to testify?

Dr. DOULL. I think the community of toxicologists has recognized for a long time that there is a significant problem in that there are many compounds of various different types, for which we have no toxicity testing data. That is a longstanding concern.

This report has documented and puts some limits on that problem, and we now know something about the magnitude of the problem. As John Bailar has said, it is clear that we are not dealing with a crisis, but it is also clear that we are dealing with a significant problem and one that we need to begin to take some steps to solve the problem.

I might just add an additional point about solving this problem. It is easier to build buildings than it is to train people, since training toxicologists takes a long time. We need, in the short term, to expand facilities and to train toxicologists and to test some of these compounds that have not been tested but the real hope for toxicology is research. We need to spend money and effort to figure out how to approach the testing with protocols that are simpler and more efficient. That is a problem for our discipline of toxicology.

Mr. PFITZER. Mr. Chairman, I just might add that I believe with regard to our level of concern, the fact that the national toxicology program requested this study and paid a considerable amount of money to get this indepth review expressed a level of concern on the part of the national toxicology program, and I would think that they now have a, at least a sound document to help them move in the direction of meeting that need.

Senator DURENBERGER. Do many of you have the opinion that new chemicals should be more thoroughly tested before they are put on the market in America today?

Dr. BAILAR. The answer is yes. I feel quite strongly that chemicals that are just coming on stream in the category of chemicals in commerce, that is, regulated under TSCA but not found in some of the other categories that we looked at, do need substanially more testing.

Senator DURENBERGER. We are often told by representatives of the chemical industry that many chemicals require very little testing because the opportunity for exposure is quite low given the intended use and the physical chemical properties. Dr. Doull, you say you are particularly concerned about the chemicals in the commerce category of chemicals. I wonder if you would explain that a little further. Do you mean that you do not know that some chemicals with widespread use are not toxic, or why is it we see a lot of chemicals in commerce?

Dr. DOULL. For the pesticides and drugs and cosmetics, we have legislation which generates a fair amount of toxicity testing for those materials. The regulations for chemicals in commerce is more recent, and therefore, we don't have as much toxicity information on these agents.

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In the past, regulatory agencies, when they lack information on a chemical, have made decisions based on the relation of that chemical to other chemicals, structure activities. When you don't have information, you do the best you can, and SAR is a pretty good way of getting a handle on what the problem may be.

What we are really saying, however, is that SAR is not the best way. The best way is to get some toxicity data on the hazards associated with the compound. The only way you do that is to get toxicity information on that compound. What we have documented in this report is the total number of compounds for which we don't have that kind of information.

I might just add one other thing quickly. We talk about old compounds that have been out there a long time and thus we don't have to worry about. An example is trichloroacetic acid. I have used TCA in my lab for 30 years, and feel that I know a lot about the toxicity of trichloroacetic acid. Someone called me recently and said they are finding trichloroacetic acid in the drinking water and asked about fetal toxicity or cancer with TCA. I looked through the literature and was astonished to find that we don't really know much about the chronic effects of trichloroacetic acid, a very old chemical. If it is in our drinking water, we need to know about the chromic toxicity of trichloroacetic acid. That is one of the old compounds we are talking about.

Senator DURENBERGER. Is the problem, in many cases, that a product comes onto the market for one use and then, over time, its use is expanded or extended to other uses?

Dr. DOULL. I think the problem has been that only certain classes of chemicals have been tightly regulated in the past. Those are the classes for which we have a lot of data. Other compounds which escape regulation, and thus have no requirement to generate tox data are the compounds that worry me.

Mr. LIVERMAN. Senator, I would like to comment, slightly off this topic, about Dr. Bailar's summary a minute ago. From the contract testing business area I want to reinforce the point which the panel members have made that it is important to increase or expand the research base. The tests that we utilize today, a long term chronic test for instance, can very well cost $700,000 and take 2 or 3 years before the results are out, and yet the belief exists, and I think I share it with my colleagues here, that there must be better methods to arrive at hazard evaluations than simply to do a long term carcinogenic test. The number that can be done is small and the amount of information and its value is limited. It is sort of indicated that there must be a better methodology, and you get that by expanding your research base and addressing the question of, what are the best methods that can be used in a routine matter to address the testing of various compounds, I think it is an important point that needs to be reinforced.

Senator DURENBERGER. When you put your drug statement together with advice on what is needed other than making some reference to the need to more widely inform the scientific community, legislators, regulators, and the public, you did not deal with responsibility in the current context. I am obviously interested in knowing what you think the role of TSCA might be in tackling the toxicity data gap that you identified.

Dr. BAILAR. I'm personally concerned that TSCA as presently written does not call for sufficient testing of new chemicals that are just coming into the commercial arena. There are some very limited requirements for testing, but they don't generally provide for a full-scale evaluation of things that may, in time, become major industrial chemicals.

Senator DURENBERGER. Any other comments? You all agree with that?

Dr. DOULL. [Nodded yes.]

Senator DURENBERGER. The lobbyists for the chemical industry have offered some criticism of your report, and I would like to get your response to a couple of them. First, that you did not count available data on chemicals that are closely related to those in your sample; for example, that you did not use structure activity in view of SAR as a surrogate for toxicity testing. What is your opinion of SAR and its limitation?

Mr. PFITZER. Mr. Chairman, I think the subject of SAR is quite clearly discussed in the priority section, because it very clearly is intended to be used there. We discussed this at considerable length in our committee, and certainly, as toxicologists, we cannot remove from our brains knowledge of closely related material. However, when one examines the data base on the quantity and quality for a particular chemical, we did not feel it appropriate to use data collected on another chemical to serve as a surrogate.

We did, however, with every chemical where there were surrogates mentioned available, look at it and consider whether or not it should be used.

Senator DURENBERGER. You probably know that EPA relies, at least that is the impression I have been getting in the last six months as Chairman of this subcommittee, that EPA relies primarily on SAR in reviewing new chemicals before manufacture because so little actual data is presented. What is your opinion of that practice?

Dr. BAILAR. It is my understanding that EPA reviews the SAR data not from choice but because that is the best they have available.

Senator DURENBERGER. What is your opinion as to whether or not that is an appropriate course of action?

Dr. BAILAR. I am not myself a toxicologist, but I understand from colleagues who are that SAR studies sometimes work very well and sometimes hardly work at all, and that you don't know how well SAR relationships hold until after you have done the testing. In other words, it cannot be used as a really good predictor in many cases.

Senator DURENBERGER. Other comments?

Mr. PFITZER. That is a good statement from a statistician and physician.

Senator DURENBERGER. Yes, let's get to the toxicologists.

Mr. PFITZER. I would say essentially the same thing. Whenever we have a new compound for which we have no data, we look at its chemical structure, and based on our experience, effects of chemicals that have some similarities, we make some preliminary judgments, and we start with that. That, in essence, is what most priority schemes start with. Since they have no numbers to deal with,

they make a judgment based on the structure. The problem is when you try to become quantitative with that estimate, there are a lot of limitations. Some of them work fairly well, and some are not so good, as John correctly said.

Senator DURENBERGER. Do you want to react to that, too? Maybe you have a specific in mind.

Dr. DOULL. It is easy to do SAR after the facts are in. When you are looking forward it is difficult. I think our report illustrates what Dr. Pfitzer is talking about. If you just look at the data and make predictions, then we get the numbers that are in that report. But if we have ten toxicologists who have been doing this for 20 years and ask them to make a judgmental report, then they may come up with a different kind of answer. That is why we can make a health hazard assessment with limited tax data.

Senator DURENBERGER. A second criticism that they have made is that you did not count, as existing, any toxicity data or exposure information that is in secret company files and that therefore you underestimated the data that exists.

Mr. PFITZER. Mr. Chairman, that certainly is true. As we have stated repeatedly in our report, we have made quantitative statements about the data that were available to us, and we recognize that we did not have access to all of it. Our dilemma, of course, is not knowing how much we didn't have, we cannot make any quantitative estimates about it. So, that is a very clear limitation to the numerical quantitative estimates.

Dr. BAILAR. May I add to that? I see a need for having toxicity data on the basis of the potential or approved use of substances, rather than on current or past use. For example, something that is on the food additive list today but is in very limited use or perhaps not in use at all, presents no hazard, but if somebody were to begin tomorrow to make and use 1 million pounds a year, we ought to have toxicity data in place today. An extension of that comment would be that when there are arguments that some substances does not require extensive additional testings because it really isn't used, although it is approved, my response is that it should then be taken off the approved list.

Senator DURENBERGER. Just staying 1 second on the issue of confidentiality, do those of you in practice or those that you know who are in medical practice ever run into problems in which a patient can be or is directly at harm because a doctor cannot get toxicity information from the manufacturer?

Dr. DOULL. I will speak from my own experience. I suspect it is not uncommon. I don't know how many people are actually harmed, but there are certainly patients that I would have treated different had I been able to get information about the toxicity of the compound to which they were exposed. What we are talking about, of course, are compounds and agents that aren't in our standard reference lists. If this happens during the daytime, we usually call the manufacturers and usually are able to get the information we need to treat the patient. If it happens at 2 o'clock in the morning, and particularly if it's a small company, then you are liable to talk to the watchman, and in that case, you go ahead and treat the patients as best you can.

Dr. BAILAR. The problem is really worse for patients when the effects are diffuse or delayed. The best example would probably be carcinogens, where the cancer may not appear for 20, 30, 40 years after exposure. The patient who develops the cancer may not remember the exposure, even if it was a substantial daily hazard. There have been a lot of intervening exposures, and it is only on a statistical basis, with long-term followup of large numbers of exposed animals or, in some cases, decades long followup of exposed people, that one is able to identify a risk that affects one group rather than, or to a greater extent than, another.

It is often very hard to link a specific medical outcome to a specific prior exposure unless that exposure is in the very recent past, minutes or hours.

Senator DURENBERGER. I have a series of other questions that would be interesting to get into, both in terms of carcinogen issues and some of the birth defect issues and so forth, but I am going to have to submit those questions to each of you in writing and ask if you will be good enough to respond to them. Again, I apologize to all of you for the delay. Despite that, I hope you won't hold it against us, because we will need your help in the future. We try to take advantage of the direction that you suggest we head in in this area.

So thank you all very much for your testimony.

Senator DURENBERGER. Our next panel includes Dr. Robert Tucker, acting director of the Office of Science and Research of the New Jersey Department of Environmental Protection and Dr. Janice Perino, manager of the Office of Chemical Safety of the Illinois Environmental Protection Agency.

We welcome you both. Your statements will both be made a part of the record. You may proceed to summarize those statements.

Doctor?

STATEMENT OF DR. ROBERT TUCKER, ACTING DIRECTOR, OFFICE OF SCIENCE AND RESEARCH, NEW JERSEY DEPARTMENT OF ENVIRONMENTAL PROTECTION

Dr. TUCKER. Mr. Chairman, I very much appreciate the opportunity to be here. From the State perspective, I think those of us who have worked in the situation having to deal directly with some of the chemical problems, Superfund sites, abandoned sites, exposure in food, really owe a debt of gratitude to those folks on the first panel and the others that participated in the National Research Council Study for bringing out the lack of information that we have. I think at the State level, when the Toxic Substances Control Act came in, we saw it as perhaps a great opportunity to get additional information and have been frustrated with its lack of working, particularly in two regards. First, it has not required enough toxicity information. In addition to the kinds of programs that the first panel mentioned, it is my opinion that the Act should be amended to require greater toxicity testing by the chemical industry, and this needs to be done with quality assurance safeguards to make sure that the data is of the highest quality.

In addition, that data needs to be reviewed. This gets to the second frustration we've had. At the State level, we haven't had

the opportunity to see some of the data for which confidentiality is claimed. It is rather frustrating to get a report back saying, deleted chemical and deleted amount that may be present in a deleted place. That is the kind of thing that we have problems with. I have been working in the State of New Jersey, which has a high population density, a high population of chemical industry, and a lot of problems, as people are aware.

Dr. Perino and I have also participated in the National Governors' Association Toxics Integration program. This is a program that is funded under a grant from TSCA, and it has allowed, I think, both of us to see that the problems in our particular States are shared all across the country. We have been meeting with people from California, Maryland, Wisconsin, and other areas, and they share the same concerns we have in not being able to get the toxics information we need.

Senator DURENBERGER. What is driving the current interest? Is it the Superfund, ground water, or something else? What is driving the current interest from the States?

Dr. TUCKER. One thing that I presented in my written testimony was our experience with the Right To Know program. We saw last year that program pass in New Jersey, finally with total support in the legislature and signed by the Governor, a result of concern by citizens about exposure, about the risks they faced. Citizen concern is probably the greatest driving force I see right now, and I see other States sharing that concern.

The problem, again, is that as our Right To Know program is implemented in New Jersey, our Department of Health has a responsibility for going out to industries and finding out what chemicals may be involved in occupational exposure, and the Department of Environmental Protection is involved in looking at environmental emissions of these chemicals and environmental exposure in the community. But we are working with finite lists. We have gotten reviews of the literature to find some chemicals that we ought to be concerned about, but as the first panel pointed out, there is this vast range of chemicals for which we have not adequate toxicity information to make a judgment as to even what we should be asking. The public wants the names of the chemicals and what they are exposed to. But what we need in addition to the names and the exposure is a real ability to assess the data for public health, and from working in these State programs, we definitely do not have that ability.

We even have problems working with chemicals for which there is some toxicity information; this has been true with PCB's, dioxin and EDB.

However, as the first panel pointed out, and as the national toxicity program study shows, there is a whole range of chemicals that have had very little testing at all, and those are the chemicals that we don't even know whether to include in our analyses.

In addition to the Right To Know, we are having problems with our Superfund sites. Actually, New Jersey had its own Spill Fund which preceeded Superfund. In fact, it was perhaps one of the models for the Federal Superfund legislation, and again, an example of New Jersey's pioneering with the toxic chemicals issue.

To get back to TSCA, there is a program under TSCA to give grants to the States. It is a small, secondary part of the Act that has been really helpful.

Our right to know program for the Department of Environmental Protection, that is, the community exposure assessment is based on an industrial survey we did in New Jersey that went out to about 15,000 industries and inquired about throughput of a list of chemicals, the exposure, dispersion in the air and that kind of information. Interestingly enough, in getting that list together and getting the legislation through the State legislature that we needed, we worked closely with the Chemical Industry Council in New Jersey and got their cooperation on how to formulate the list. We have had significant cooperation from the industry and much less problems with confidentiality than I would have expected. We have had very few requests for confidentiality on the information that we have asked for.

That makes me wonder whether some companies resort unnecessarily to the confidentiality provisions under TSCA. I sometimes have a suspicion that, one, it is partly a way to get around or to tie up the regulations; and second, I think the confidentiality regulations are used as a way to avoid liability. I think that is a misuse of the confidentiality concept.

Senator DURENBERGER. I might add a third as a former lawyer for a specialty chemical company, and that is I could see where you could be successful because they could see a particular end use. They knew why you wanted that information, why you needed the information, why it was important. It seemed to me 10 years ago or so when I was first addressing this issue, the presumption was that a lot of confidential information and very competitive information would end up in large boxes some place in Washington that nobody really cared and that the Government was just doing it because it was the Government.

But one of the interesting things I noted in reading the study that these folks put together over the weekend is that there are tons of this material sitting over at FDA, for example, and they can't even find it, let alone a competitor. So that might be a third reason.

If we could ever focus, as we are apparently trying to do here today, on why we need this information, perhaps we could get the same kind of cooperation from the industry that you find in New Jersey.

Dr. TUCKER. Yes. It is a point very well taken that the information, if it exists somewhere, is not available whether through neglect or poor recordkeeping or secrecy or whatever. But my impression from New Jersey is that there is now a very different climate among the public in wanting this information. Our experience with the right to know is that people really are concerned about chemical risks. It is not a panic situation; it is not a crisis; but it is a very great concern on the part of people to know what is in their environment, what is coming out of the stacks and what is in their food.

Speaking from the state level, I think there are some industries that are very much more responsible than others. Some companies are making an effort to make toxicity information known, and

others aren't. I have heard colleagues from the chemical industry blame the public for having chemophobia, a nonsensical fear of chemicals. To some extent I think this can be laid to some of the past practices of the industry and to their advertising, where with some kinds of slogans they have tried to take advantage of the mystique of difficulty with chemical names by using the authority of a model such as a doctor or a pharmacist saying, "This stuff is good for you, but we won't tell you what it is." I think that has caused a problem in the public perception and some concern.

I think what the public is reacting now to is that past lack of information and realizing that there is a need to know what they are exposed to and demanding this information.

Again, I think the study that we heard about from the first panel has been a marvelous study and a real service to the public.

Senator DURENBERGER. Thank you very much.

Dr. PERINO.

STATEMENT OF DR. JANICE PERINO, MANAGER, OFFICE OF CHEMICAL SAFETY, ILLINOIS ENVIRONMENTAL PROTECTION AGENCY

Dr. PERINO. Good afternoon Mr. Chairman and members of the subcommittee.

I am Dr. Janice Perino. I am manager of the Office of Chemical Safety for the State of Illinois for the Illinois EPA. I am appearing today on behalf of Mr. Roger Kanerva, manager of the environmental programs. His written testimony is presented for the record at this hearing. He asked me to expresss his regrets for his absence. Last minute events at home prevented his attendance here today.

We are participating today to share our concerns about some very troublesome times ahead regarding adequate control of toxic chemical substances. We are concerned about the ability of the current regulatory system to deliver what the public wants today in terms of environmental protection: assurance that it is indeed "safe" from toxic chemical substances.

In our written testimony, we provide some data about toxics in Illinois and report on what we call the "race to know." We point out that the regulatory system faces a great challenge in responding to public inquiry about the potential adverse effects of all chemical substances, and that reflects on New Jersey's comments.

We stress that there is an urgent need to understand what all this blizzard of information about toxic means for citizens, business, and public officials. To this end, we report on the results of a 2-year project in Illinois which culminated in the recent publishing of a strategy titled "Chemical Safety: An Agenda for Continued Progress in the Control of Toxic Pollutants." And I would like to submit this for your consideration.

Senator DURENBERGER. It will be made a part of the record. (See p. 76.)

Dr. PERINO. This agenda presents a blueprint for achieving a better understanding about the environmental and public health impacts of toxic chemical substances, and, eventually, enhanced control procedures.

The Illinois effort appears to be particularly timely, given the status of related events at the national level, especially the report that we just heard about. The National Academy of Sciences recently published a report on the status of toxicity testing. Their finding of a shortfall in the national arena represents perplexing news from a State perspective. While we plan to address site perspective of toxicity problems in Illinois, we must look for support and assistance from the national testing programs to augment our toxics data-base needs. Without similar productive efforts at the national level for new and existing chemicals, we would appear to be caught in an endless loop of always being one step behind the next round of problems. And certain States are aware of the effects on our State budgets and our State activities when this occurs.

The chemical safety agenda has also served to focus attention in Illinois upon the need for "good government" to combat toxicants. There is a pressing need for more technical expertise and better integration of program activities to achieve improved toxicity control. In Illinois, this need resulted in the creation of the Office of Chemical Safety by Gov. James Thompson.

But we cannot operate in a vacuum in Illinois regarding toxics control. We believe that better use can be made of TSCA as an umbrella mechanism for coordination and integration of toxic control activities. TSCA could serve as a powerful tool for buttressing the information weeknesses of other environmental management programs. However, we also feel that TSCA can be improved to make better use of the Federal/State partnership.

I would like to thank you for including Illinois in the hearing today. I would be pleased to respond to questions or to supplement the record at a later date if you so desire.

Senator DURENBERGER. I thank you very much. I think both of your statements probably tell us where some of the problems or views are coming from. Both of them highlight what many of us ought to know if we read our hometown newspapers, and so forth, and that is the incredible public level of concern that for some reason or another misses a lot of appropriators around this place.

I was curious to know, Dr. Perino, and maybe you didn't come equipped with the answer, but one of my recent reviews of a newspaper clipping from Minnesota showed 175 railroad cars of contaminated earth from a lumber company in Minnesota being turned away from a hazardous waste site in Illinois for some alleged fear that it contained dioxin. Do you know anything about that situation?

What caused it? How did it come about?

Dr. PERINO. I will summarize what I know about the situation. I can look into that and submit information to you later, but that is why we are in this sort of a situation.

Senator DURENBERGER. Illinois, in addition to problems that you set out in your statement in terms of being the fifth largest generator and so forth, I take it, is also currently the recipient of other people's problems from States that haven't addressed the issue of hazardous waste disposal. Is that right?

Dr. PERINO. That is.

Senator DURENBERGER. You seem to be saying in your statement, Dr. Perino, that TSCA should be or could be used as a tool to make

all the other chemical regulatory programs work better. Could you elaborate on that point?

Dr. PERINO. Yes. There are several kinds of ways that we would like to see TSCA help us in our State programs, things like determining how clear is clean? Within our existing programs of the air, water, land and public water supplies, we have some information about chemicals, but oftentimes, very little about what the toxicity is of those chemicals, making it unrealistic for us to try and control or to improve the situation for the citizens and for the environment of the State.

The health significance of contaminants in drinking water is a problem that we do not know answers to, and we don't seem to be getting answers to them.

Senator DURENBERGER. Dr. Tucker, you called for additional testing under TSCA, and some testing, as we all know, is already being conducted on priority chemicals that are identified by the Interagency Testing Committee. Is it your testimony that that is not enough?

Dr. TUCKER. I think the National Research Council study clearly shows that that is not enough and that we obviously need more testing. If close to 90 percent of chemicals in general use do not have adequate toxicity information there is clearly a need for additional testing.

Senator DURENBERGER. Dr. Perino, from the Illinois perspective, and I have already heard some of this from New Jersey, but could you elaborate a little bit on confidential business information problems as you see it in Illinois?

Dr. PERINO. You know, we know we have a problem in the State of Illinois for not being able to get that information, but I think it's a two-way street. I think that the U.S. EPA's program in TSCA would go more smoothly if they could share that information with us. They are faced with a situation where they can't get information from us because they don't know what to ask about a particular situation. We are faced with the inability to make the best decisions we can, both for industry and the citizens in the State because there are so many gaps; there are so many gaps in the confidential data, and we have methods for handling the confidential data, also.

But it is not available to the States at all. Permitting programs, programs that can involve questions of special toxicants if the State were not able to receive that information from TSCA, and we could do a better job if we could.

Senator DURENBERGER. Dr. Tucker, the Academy report estimates that 64 percent of pesticides have either no human toxicity data or less than minimal data. What is your opinion as to whether or not pesticides with a lack of human health data should be continued in use?

Dr. TUCKER. In my opinion, pesticides represent a particular problem because of their likely widespread environmental exposure, the likelihood of innumerable routes to human exposure, whether through getting on produce or into the food chain and then the human food supply, or through the kinds of problems we have had with ground water contamination, such as with DBCP or

other pesticides. Not only is it the toxicity information that we lack but information about the environmental fate of pesticides.

I would be very reluctant to see the use of pesticides without that kind of adequate information. I think it is uncalled for to have pesticides used with their potentiality for wide spread human exposure without adequate testing.

Senator DURENBERGER. OK. I thank you both very much for your testimony, your written testimony and your oral testimony and the responses.

The hearing will be adjourned.

[Whereupon, at 4:32 p.m., the hearing of the subcommittee was adjourned, subject to the call of the Chair.]

[Statements and other material supplied for the record follows:]

10 April 84
Statement by John C. Bailar, III, M.D., Ph.D.
Department of Biostatistics, Harvard School of Public Health

In 1980, the National Toxicology Program (NTP) contracted with the National Academy of Sciences (NAS) for a study with two main charges, which might be simplified and paraphrased as:

a) To characterize unmet needs for testing the toxicity of substances with known or expected human exposure, and
b) To develop criteria for setting priorities for future testing.

In response to these charges the NAS appointed a Steering Committee under Dr. James Whittenberger and three topic-oriented Committees. Members of today's panel come from the two Committees that dealt with the first charge. I was chair of the Committee on Statistical Sampling Methods, and Drs. Doull and Pfitzer were Co-Chairs of the Committee on Characterization of Status of Toxicity Data Elements for a Select Universe of Compounds. The third arm of this effort, the Committee on Research of Agents Potentially Hazardous to Human Health, under Dr.Arthur Upton, dealt mainly with the second charge and is not represented here.

During the three years of the study the task of my committee grew from a narrow focus on study design to include an active role in interpretation of the data. Our two groups drew more and more closely together over time, so that in the end we functioned almost like a single committee, we wrote a single report, and the three of us today will present different parts of our common effort. I will describe the structure of the study and comment on the validity of conclusions, Dr. Doull will discuss the salient qualitative aspects of the findings, and Dr. Pfitzer will summarize some of the critical quantitative findings.

More than five million chemical compounds have been described in the scientific literature, and the list continues to grow rapidly. Most of those compounds, however, are made only in laboratory quantities, or for other reasons could have little or no effect on human health and survival. Also, resources did not permit a search of the whole five million substances to determine which ones might be of public health interest. We therefore focused attention on <u>existing lists</u> of chemicals that had at least one of three characteristics:

many or most items on the list were thought to be made in substantial quantity, or
the list contained a high proportion of items selected because of close, frequent, or prolonged human exposure, or
the list contained a high proportion of items selected because of known, substantial biologic effects.

In the end, we worked with five such lists, which, taken together, contain a high proportion of chemical substances likely to threaten life or health in the United States. The lists were:

the NIH/EPA Chemical Information System (CIS) lists of registered active pesticides and inert ingredients for use in pesticide products,
a list of cosmetic ingredients maintained by the Cosmetic, Toiletry and Fragrance Association

the FDA list of drugs and excipients in drug formulations
segments of the FDA chemical dictionary containing approved food additives
EPA's list of "chemicals in commerce", generally those produced in quantities of at least 1,000 pounds per year by at least one manufacturer

The list of chemicals in commerce was subdivided into three parts on the basis of total production volume (under 1,000,000 pounds per year, over 1,000,000 pounds per year, and volume unknown to us). Altogether, these lists contained 65,725 entries representing about 53,500 separate substances after the removal of duplicates.

Even this reduced number of chemicals was far too large for us to consider individually. We therefore drew statistically valid random samples from each list. Sample sizes varied from 50 (drugs and excipients; pesticides and inert ingredients), to 100 (cosmetic ingredients; food additives), to 125 (each part of the list of chemicals in comments). Items on these samples were studied for the simple presence or absence of several critical kinds of data, without regard to whether the data were good or bad. This is evaluation in its simplest and crudest form: if someone reported that a study had been done, we counted it. Substances that were found to have at least a minimal amount of toxicity information (separately and precisely defined for each list) were eligible for inclusion in a second-stage sample for much more detailed study. Altogether, 675 substances were chosen for the initial sample, and 100 of these, spread over the seven lists and sub-lists, were chosen for the second-stage sample.

Drs. Pfitzer and Doull will describe what was learned from these samples. I will continue my remarks now be describing certain aspects of the study context and procedure. First, we should remember that our goal was to assess the state of knowledge about toxicity, not to tabulate what kinds of toxicity had or had not been found. Thus, we cannot tell you (for example) how many chemicals in commerce are carcinogens. Second, we have good reason to believe that some information was filed in old records of both industry and government, but was not or could not be made available to us. Our approach to this matter was that if we couldn't see the data, others probably could not see the data either, so that the study was of no current value in assessing the hazards of an item on these high-volume, high-exposure, high-impact lists. Thus, in an operational sense, if we could not see the data, the data effectively did not exist.

Third, there were severe constraints on sample sizes, especially at the highly labor-intensive second stage of sampling. We learned quite early that no more than 100 substances could be fully studied by the committee, even over this 3-year study, and we deliberately chose to spread those 100 over all 5 lists (or 7 sublists). We though it better to learn a little about each major area rather than to learn a lot about just one or two areas. And fourth, because of the way our samples were drawn, inferences at this time are limited to lists. For example, our tabulations refer to drugs and drug excipients combined, not to drugs alone.

What, then, can one learn from this study, especially when samples are small and statistical confidence limits are wide? One can in fact learn a great deal, because of three critical features

of the data. For one thing, the second-stage findings tended generally to support and extend findings from the much larger first-stage samples. Both showed serious and widespread gaps in knowledge about the toxicity of chemicals that are common in our daily lives. When the first and second stages are considered together, conclusions are seen to be solidly based.

The next general point is that findings from the separate parts of the second-stage sample strongly reinforce each other. If one were to find something in a sample of just 10 or 15 chemicals, one might tend to dismiss it, but that is harder to do when the same finding appears in a second sample of 15, and again in a third, and so forth. All seven parts of the second-stage sample, small as they were, showed serious gaps in toxicity knowledge available to protect the public.

Finally, even the very wide confidence limits on our results may have their uses. If we estimate, for example, that some critical test of drugs has been performed for between 5% and 60% of drugs and excipients (e.g., human sensitization studies performed according to reference protocol guidelines, pages 104-105), the person who thinks the figure should be close to 100% will not be satisfied. Again, we believe that these small samples do establish some critical gaps - big gaps - that should not be there.

BIOGRPAHICAL SKETCH

My name is John C. Bailar, III. I am a physician (M.D., Yale 1955) and statistician (Ph.D., American University 1973). I spent 22 years in various scientific and managerial positions at the National Cancer Institute (NCI). For two years I directed the national research program of the Veterans Administration. Since 1980 I have been Lecturer in Biostatistics at the Harvard School of Public Health as well as Statistical Consultant for the New England Journal of Medicine. For about three years, overlapping my time at both NCI and Harvard, substantial parts of my professional duties were in the Office of Toxic Substances, Environmental Protection Agency. I have published more than 150 original papers, reviews, and abstracts in the medical and scientific literature. My special interests are in the assessment and appraisal of risks to human life and health, aspects of environmental health policy, and methods to design and interpret research studies when the data are subject to substantial uncontrollable error.

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United States Senate
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS
WASHINGTON, D.C. 20510

April 13, 1984

Dr. John C. Bailar
Lecturer in Biostatistics
Harvard School of Public Health
Department of Biostatistics
677 Huntington Avenue
Boston, Massachusetts 02115

Dear Dr. Bailar:

Thank you again for your testimony at the recent hearing on toxicity testing. Yours was a valuable contribution to our understanding of this important subject. Due to the constraints of time, however, we were unable to address all the questions I wished to ask. Therefore, I would appreciate your written responses to the following questions.

Please respond by April 30, so that we can proceed with publication of the hearing record.

Sincerely,

Dave Durenberger
Chairman
Subcommittee on Toxic Substances
and Environmental Oversight

enclosure

QUESTIONS FOR DR. BAILER

1. You call for an updated survey of testing capacity and use of priority setting mechanism to determine which chemicals to test. Dr. Liverman made a similar recommendation.

- Do you mean that we should continue testing as we are not until these tasks are accomplished?

- What should be the role of TSCA in tackling the toxicity data gap identified in the NAS report?

2. The results of the NAS study are a direct challenge to public confidence in assuming that the chemicals we come in contact with daily are safe. Figure 2 of the study particularly sparks concern about the adequacy of controls governing substances in the market place.

- In your opinion, is there a correlation between the amount or adequacy of toxicity testing on various chemicals relative to the actual risk that they may pose to health and the environment?

- Is the absence of toxicity data on the preponderance of substances because in fact they do not readily exhibit signs of being toxic, or is this an artifact of the lack of controls to trigger testing?

- Are there conclusions to be drawn from the absence of complete health hazard assessments on chemicals in commerce? Specifically, can the untested substances be presumed to be benign?

- In defining a "complete health hazard assessment", was neurotoxicity testing a criteria?

3. As a policy matter, do you believe that mandatory testing of at least some types of new chemicals and new uses of existing chemicals should be required before they can be marketed? If so, please comment on the concepts of either a tiered testing scheme or base set of testing. Recognizing the great diversity of chemicals and use/exposure situations that may lead to health risk from new chemicals or new uses of existing chemicals, do you think that government or industry should bear the burden of persuasion concerning the need for testing in these cases?

468 N Street, SW
Washington, DC 20024
24 April 1984

The Honorable Dave Durenberger
United States Senate
Washington, D. C. 20515

Dear Senator Durenberger:

Thank you for your letter of 13 April asking for written responses to several questions. My replies, keyed to your questions, are enclosed.

There is a serious problem with incomplete and inadequate testing of potentially toxic chemicals, and there is a distinct possibility of a public health disaster at some future time. I am very glad indeed that you have taken an interest. Please write or telephone if you see any way that I can help to move things ahead.

Sincerely,

John Thurston Bailar III

John C. Bailar, III, M.D., Ph.D.
Lecturer in Biostatistics
Harvard School of Public Health

Enclosure

I.A. I believe that all members of our panel found a need for both a) an updated survey of testing capacity (what can be done) and b) better ways to set priorities for testing (what should be done).

There is some degree of slack in present testing capacity, but it is clear also that even full use of present capacity would not be enough. It would be foolish to allow existing, needed facilities to sit idle, or to hold off on developing new facilities that will quite clearly be needed, while we wait for a survey to tell us that we will need even greater expansion in laboratories, trained personnel, and the rest.

It is clear also that present priority-setting mechanisms work reasonably well (though not well enough), and that they rarely or never assign high priorities to testing chemicals that improved priority procedures would leave out of the running.

Thus, neither the need for the survey or the need to implement better priority mechanisms should delay testing that we know can and should be done now. Let's get started as promptly as possible.

I.B. TSCA is one of several important regulatory tools for improving knowledge about toxic hazards and, in time, abating those hazards. I see a need to strengthen the hand (and perhaps the spine) of EPA in dealing with each of the broad classes of chemicals regulated under TSCA. Two specific points to consider for change are the present need for EPA to show evidence of a possible hazard from a new chemical in commerce (TSCA, Section 5) before it can require testing relative to that hazard, and the very slow and expensive process for requiring additional testing of major industrial chemicals (Section 4) when there is substantial, specific reason for concern.

II.A. The NAS study, with very limited sample sizes, was unable to show a correlation between production volume and the extent of information on health hazards in TSCA chemicals as a whole. That result was somewhat surprizing, and I suspect that larger samples would show at least some correlation between volume and testing. Production volume, however, is not the only determinant of risk. Two features that are likely to be even more important are prolonged, direct human exposure (as with drugs, food additives, and cosmetics), and commercial production of a chemical because of its proven biologic effects (as with drugs--again--and pesticides). The NAS data do show these classes of substances have been studied more than run-of-the-mill TSCA chemicals. My overall opinion is thus that there is some degree of correlation between risks to health and the amount and adequacy of testing, though that correlation is not nearly as great as it should be.

Your question also asked about risks to the environment, but I do not feel qualified to comment on that point.

II.B. One can only guess at the extent to which past decisions about toxicity testing were influenced by beliefs (and even data) that certain

substances were or were not likely to be hazardous. It is entirely plausible that the vast majority of manufacturers would insist on adequate testing of each manufactured substance that was really under suspicion. It is equally plausible, I fear, that a handful of manufacturers would rather not hear any bad news about a currently or potentially profitable product, and that needed testing might therefore be omitted, incompletely reported, or misinterpreted.

The problem is compounded by the fact that some kinds of hazards (carcinogencity is the best example) are very difficult to detect and prove from unstructured observations of exposed humans. Some kinds of major chemical hazards might well be unsuspected and hence not investigated by even the most conscientious manufacturer and/or regulatory agency.

II.C. You ask whether untested substances can be presumed to be benign. The answer is a firm and unequivocal "No." That is not to say that they are all equally in need of testing; a good priority system would sort them out according to several critical features: the expected nature and extent of human exposure, any biologic effects already known, probable production volume, physical properties, toxicity of chemically related substances, and perhaps many other things.

II.D. The Committees considered the availability of test results for two kinds of neurotoxicity: acute delayed neurotoxicity and subchronic neurotoxicity. In summary, data on acute delayed neurotoxicity were considered necessary for a complete health hazard assessment for occupational and environmental exposures to pesticides and TSCA chemicals, and for a few drug uses. Data on subchronic neurotoxicity were considered necessary for some kinds of food additives, some classes of drugs, pesticides, and TSCA chemicals.

Requirements for neurotoxicity testing were in practice a little more complicated than this; Drs. Doull and Pfitzer could supply details. (This question and response illustrate the care used in determining whether a complete health hazard assessment was possible. Across-the-board definitions were avoided in favor of definitions based on class of substance, intended uses, and probable levels and routes of human exposure.)

III. I am convinced that each new chemical, or each new use of an older chemical, should be carefully reviewed within a comprehensive priority structure to determine whether, and what, testing is necessary. It might well turn out that a proportion of new substances and new uses might be found to have relatively low priority for testing because of such things as low expected production volume, lack of significant human exposure, or prior biological/biochemical information on closely related

chemicals that risks are almost certainly tiny. An example might be a possibly toxic monomer locked in an inert, insoluble polymer. Rational decisions to limit or omit testing might, however, depend heavily on matters that cannot now be given adequate weight in premanufacture or premarketing reviews, or may change after regulatory approval of some substance or use. Examples are a finding that actual production methods or volumes differ substantially from those projected at the time of approval, or new knowledge about the toxicity of related substances. Some types of new chemicals and new uses should certainly be subject to mandatory testing -- but not all of them. Hence a need for priorities.

You asked about tiered testing and base-set testing. This question seem to have greatest relavance to TSCA chemicals. There would be much benefit in having well-developed testing schemas for TSCA chemicals, as there are now for chemicals regulated under other laws, but it may well be that the structure of the schema (tiered, base-set, or other) would vary from one broad class of substances to another. One might, just as an example, require a simple base set of tests for chemicals not produced in excess of 50,000 pounds per year by any manufacturer, a more complex base set up to 1,000,000 pounds, and a tiered system for higher volumes. Or, again just to illustrate, one might have a tiered system for aromatic hydrocarbons and a base set for all other compounds.

You asked also whether the burden of persuasion should be on government or industry. I see no alternative to leaving on government the burden of assuring that adequate testing is done, though this does not mean that government should actually do more than a very small part of the needed testing. Most of the industry is, I believe, quite responsible about both investigating and reducing demonstrated risks to human health, but I see several problems in leaving industry to lead this effort: insufficient incentive to test for hazards that are suspected only vaguely, or not at all; lack of knowledge about both possible risks and methods of testing by many small manufacturers; the small proportion who would act in bad faith; even the need to maintain public confidence in an industry sometimes viewed with suspicion.

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ROCHE RESEARCH CENTER

May 1, 1984

The Honorable Dave Durenberger
Chairman, Subcommittee on Toxic
Substances and Environmental Oversight
Committee on Environment and Public Works
Washington, D. C. 20510

Dear Senator Durenberger:

Thank you for the opportunity to present a statement at your recent hearing on toxicity testing. As requested, I am providing responses to the additional questions in your letter of April 13.

Sincerely yours,

Emil A. Pfitzer, Sc.D.
Director
Department of Toxicology
and Pathology

EAP/lv

Attachment

cc: Dr. J. Bailar
Dr. J. Doull

QUESTION FOR DR. PFITZER

1. We have been hearing more and more lately about chronic effects other than cancer. I am thinking specifically of birth defects, reproductive dysfunction, and neurotoxicity.

- Do you think these effects are important too?
- Are they common?
- Are there tests that can be run on chemicals to predict each of these effects?

2. You call for an updated survey of testing capacity and use of priority setting mechanism to determine which chemicals to test. Dr. Liverman made a similar recommendation.

- Do you mean that we should continue testing as we are now until these tasks are accomplished?
- What should be the role of TSCA in tackling the toxicity data gap identified in the NAS report?

1. Birth defects, reproductive dysfunction and neurotoxicity are extremely important potential toxic effects of chemicals. While these effects are relatively common, their etiology is often uncertain and the incidence due to chemicals in the environment is often debated. Nevertheless, the prevention of chemical exposures that may cause such effects must have high priority. Our state-of-the-art procedures are quite good for predicting birth defects and reasonably good for predicting reproductive dysfunction. Certain types of neurotoxicity can be predicted reasonably well, but other types, particularly neurobehavioral changes, are subjective and subtle effects are very difficult to predict.

2. Even though there are currently increases in toxicity testing, there is also an increase in production of new chemicals. If we continue to test for the toxicity of chemicals as we do now, we will only get further behind with the large number of chemicals in commerce for which little or no information is available. Of course, we should not let up on our current efforts while new procedures are evaluated. TSCA should define more specifically the toxicity tests required for chemicals under its jurisdiction. This might be done using strategies recommended to NTP. A major lack is exposure information that could assist in deciding whether or not testing is needed.

RESPONSES FROM JAMES L. LIVERMAN

QUESTION 1. I sense difficulty is being encountered in defining the components of the industry devoted strictly to testing for the hazardous nature of chemicals and therefore in refining estimates of actual available capacity. I have two questions:

a. What is your recommendation for refining these parameters?

b. Would you and your associates be prepared to work with the Committee staff and with your colleagues from this panel in fashioning a practicable but visionary program of government and industry cooperation to the end that we might more quickly whittle down the large number of chemicals about whose toxicity we know so little.

ANSWER:

a. I strongly recommend an updating of the 1981 study with more rigorous definitions of the components of the testing industry prepared to do testing under Good Laboratory Practice Regulations. Such a definition would not eliminate any components of the 1981 study but it would give a more realistic estimate of the parts of the industry prepared to devote all its efforts to the safety testing. Particular effort should be taken to delineate the criteria for classification of the various kinds of laboratories so that it is possible to differentiate clearly between those labs which have historically and will continue to be principally in testing and those which principally do research and develop test methodology with testing only a small part of their objectives. It is also important that those ultimately responsible for policy direction be consulted regarding the future efforts of the laboratories. For instance, in what categories should the various government, GOCO, and university laboratories be placed, i.e., will they be focused on testing or will their objectives be only peripherally concerned with testing? These kinds of questions must be answered in a survey to give an accurate measure of available capacity and define the conditions under which it will be available.

b. From discussions I have had in the toxicology community the answer is a definite yes. Certainly NALSI is ready to assist in any way that it is possible to help evolve a program with the right balance of capability, capacity, commitment and financing in order to mount a well planned attack on reducing the uncertainty surrounding the large numbers of compounds not yet evaluated from the hazard standpoint.

QUESTION 2: Beyond the approximately 30%-50% additional laboratory testing capacity that now seems to be available in the contract testing laboratories, what are the principal factors inhibiting the further expansion of facilities which may be needed to reduce the numbers of chemicals to be tested to a more comfortable number in a shorter period of time?

ANSWER:

I believe a first and essential step is for the government to develop and maintain a consistent policy on testing requirements. So long as the industry

does not feel that there exists a constant enforcement so that all companies are treated equally, they could be placed at an economic disadvantage to do nonrequired testing.

Certainly a second important step is to saturate the estimated excess testing capacity that does exist. If there is still a demand for capacity above and beyond that which exists, the survey suggested in response to Question 1 above should reveal opportunities in places such as the surplus capacity in various GOCO facilities caused by cutback in federal support of research. Such places should be operated in a manner that they do not compete unfairly with those commercial testing companies that have provided the capital for facility investment, otherwise the testing industry which is the ultimate backbone of the capability to maintain an adequate base will ultimately go out of existence for lack of incentive.

Finally, if additional facilities are still needed, I believe the commercial testing industry will provide those dependent only upon a declared national goal that the testing must be done. The uncertain drum of regulatory requirements in recent years have slowed that determination of the commercial industry to make provision for facilities since there was no incentive to invest.

QUESTION 3. The NAS report variously refers to acute, chronic effects, etc., in the studies which are conducted. Could you identify the components of testing, especially those factors which dictate the length and complexity of the tests?

ANSWER:

The principal value of acute tests which normally involve a single exposure to a chemical with observations extending over perhaps two weeks is to determine toxicity over a wide range of doses. From these results one is able to set the dose levels for subchronic and chronic studies. Costs for acute studies usually range from $500-$2000 depending upon the mode of treatment, etc.

Subchronic studies are ones in which the aim is to determine broad general effects on development of embryos, on reproduction, on behavior, various malformations, etc., along with gross pathological events in tissue. These studies make use of information on dose from the acute studies and generally extend for 90-120 days and cost from $30-100,000 depending upon the species, method of exposure, etc. Additionally these studies give a more precise definition of the appropriate dose range and kinds of observations that need to be made in a longer chronic study.

Chronic studies are aimed at determining the effects of doses that would overlap those to which man might be exposed and to look at all important endpoints including in a major way cancer occurrence. These studies are ones that extend from 180 days to 10 years depending upon the particular chemical being studied. The 10 year studies generally have involved birth control medication etc., and usually involve nonhuman primates. Most studies are done with mice, rats, and small animals and usually run from 180-700 days, and cost from $300,000 to $1,000,000 depending upon the experimental protocol.

QUESTION 4: In vitro testing has been mentioned. Please explain in lay terms what is meant by the term and mention a test or two. Could you also address briefly why it is necessary to also do tests using live animals, especially in the context of extrapolation of results to man.

ANSWER:

In vitro testing is a term used to describe a group of tests that do not involve whole animals, rather it is testing using microbial, bacterial, animal or human tissue systems or combinations of these systems with whole animals. Usually these tests are done in small dishes, test tubes, etc. Perhaps the best known of this group at the present is the Ames Test which involves evaluation of the mutagenic potential of various chemicals in a microbial system wherein the chemical is pretreated with rat liver enzymes to determine if passing through the animal system may modify the compound to the degree that it become mutagenic or nonmutagenic.

There is a current vigorous push to decrease the numbers of animals used in experimentation and replace those tests with in vitro tests. It is certainly a fact that much can be gained by the additional knowledge that can come from in vitro tests but the current regulatory requirements cannot be met by such tests. The consensus is that for some time chronic animal studies will be needed to determine carcinogenicity, that definitive determination of behavioral effects, of effects on vision, etc., cannot be determined by in vitro means. Thus, the need I referred to earlier in my testimony for detailed and continuous evaluation of experimental results to determine the most appropriate set of tests to be run to evaluate hazard of chemicals.

Toxicity Testing

Strategies to Determine Needs and Priorities

Steering Committee on Identification of Toxic and Potentially Toxic Chemicals for Consideration by the National Toxicology Program

Board on Toxicology and Environmental Health Hazards

Commission on Life Sciences

National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1984

EXECUTIVE SUMMARY

Abstract: A "select universe" of 65,725 substances that are of possible concern to the National Toxicology Program (NTP) because of their potential for human exposure was identified. Through a random sampling process, 675 substances covering seven major intended-use categories were selected. From this sample, a subsample of 100 substances was selected by screening for the presence of at least some toxicity information. In-depth examination of this subsample led to the conclusion that enough toxicity and exposure information is available for a complete health-hazard assessment to be conducted on only a small fraction of the subsample. On the great majority of the substances, data considered to be essential for conducting a health-hazard assessment are lacking. By inference, similar conclusions were made for the select universe from which the sample and the subsample were drawn. This report presents criteria for selecting substances and determining toxicity-testing needs, provides estimates of those needs, and describes some useful criteria for assigning priorities for toxicity testing.

The potential public-health impacts of chemicals lead society to seek information for determining the probability and magnitude of such impacts. Such information is based primarily on predictions from results of toxicity studies. The development of a strategy for obtaining appropriate information requires an estimation of the quantity and quality of available toxicity data applicable to the assessment of human health hazard, as well as knowledge of the number of substances on which necessary experimental data are not yet available. A characterization of the magnitude of needed testing would be valuable to those who allocate resources for such testing. However, because resources for developing sound scientific bases for identifying public-health hazards are limited, it is important to establish priorities among chemicals and to select those known or expected to have the greatest impact on human health.

A major function of the National Toxicology Program (NTP) is the selection and testing of chemicals for toxicity. NTP has under continuing review candidate chemicals for testing, as they are nominated by the federal agencies served by the program, by state and local governments, and by academic, industrial, and labor groups. Such candidates are of interest to NTP because of their potential for human exposure and public-health impact.

In September 1980, NTP, through the National Institute of Environmental Health Sciences, contracted with the National Research Council (NRC) of the National Academy of Sciences for a study. This study was undertaken because NTP recognizes that the number of substances, both natural and man-made, in the human environment is very large and is increasing, with no clear indication of the nature and amount of toxicity information that might be needed on these substances

to ascertain their potential for adverse effects on human health. It is useful for NTP to know as precisely as practicable the toxicity-testing needs for substances to which humans are potentially exposed.

NTP asked NRC to address these matters in two major objectives of the study:

(1) To characterize the toxicity-testing needs for substances to which there is known or anticipated human exposure, so that federal agencies responsible for the protection of public health will have the appropriate information needed to anticipate the extent of testing needs.

(2) To develop and validate uniformly applicable and wide-ranging criteria by which to set priorities for research on substances with potentially adverse public-health impact.

The study, titled "Identification of Toxic and Potentially Toxic Chemicals for Consideration by the National Toxicology Program," was established in the Board on Toxicology and Environmental Health Hazards of the NRC Commission on Life Sciences.

In this report, the Committee on Sampling Strategies and the Committee on Toxicity Data Elements describe in detail the criteria and procedures they used to determine the nature and extent of toxicity testing and their collective judgment on the testing needs for a "select universe" of chemical substances. The underlying strategy for the characterization of toxicity-testing needs involved four major steps:

(1) Definition of the select universe of substances that might be of interest to NTP because of their potential for human exposure.

(2) Drawing of a random sample of representative substances from the select universe.

(3) Statistical analysis of the sample to determine the quantity and quality of available information and detailed description of testing needs for the sample.

(4) Predictions, based on the sample analysis, of the testing needs for the select universe.

The Committee on Priority Mechanisms presents criteria and a decision-making framework that could be used to set priorities for research on substances with a potential for adverse public-health impact.

SELECT UNIVERSE OF SUBSTANCES

According to an estimate based on the Chemical Abstracts Service (CAS) Registry, the universe of known chemicals consists of over 5 million entities. To define toxicity-testing needs for substances in the human environment, it was necessary to select a manageable subset of the universe that would include most of the substances to which humans are likely to be exposed in the United States. The construction of this "select universe" of substances--a core that would be the reference for the study--relied on a search for lists of substances preselected for human exposure potential and computerized for reasonably easy access. A search for such lists revealed several that could be assembled to form the select universe, provided that most duplications of substances on the combined lists could be identified to permit statistical adjustments. The lists used included the Toxic Substances Control Act (TSCA) Inventory of 48,523 chemical substances in commerce; a list of 3,350 pesticides (active and inert ingredients) registered for use by the Environmental Protection Agency (EPA); a list of 1,815 prescription and nonprescription drugs approved by the Food and Drug Administration (FDA) and excipients used in drug formulations; a list of 8,627 food additives, including those approved for use by FDA; and a list of 3,410 cosmetic ingredients from the Cosmetic, Toiletry and Fragrance Association. This select universe did not systematically include environmental decomposition products, manufacturing contaminants, or natural substances (e.g., plant pollens and foods). The sum of the above, 65,725 entries from the lists, was taken as the select universe for the purposes of this study. Statistical adjustment for duplications indicated that the select universe contained about 53,500 distinct entities. The Committee on Toxicity Data Elements and the Committee on Sampling Strategies regarded the contents of the select universe as closely approximating the expected universe of interest to NTP.

CHARACTERIZING TOXICITY-TESTING NEEDS

During the planning stages of the study, it was recognized that the Committee on Toxicity Data Elements would not be able to examine the information on all 53,500 substances in the select universe, because of limitations of available resources. Therefore, the Committee on Sampling Strategies developed a method for drawing from the select universe a sample that was (1) small enough to be thoroughly examined for completeness, quality, and utility of information within the limitations of available resources and (2) designed to permit an extension of the committees' findings from the sample back to the select universe from which it was drawn. With a stratified random process, 675 substances were selected from the 65,725 listings. A random subsample of 100 substances with at least minimal toxicity information (described in Chapter 2 of Part 1) as prescribed by the Committee on Toxicity Data Elements was then selected from the random sample. The select universe, the sample, and the subsample contained representatives of seven categories of substances

defined by the lists that make up the select universe: (1) pesticides and inert ingredients of pesticide formulations, (2) cosmetic ingredients, (3) drugs and excipients in drug formulations, (4) food additives, and chemicals in commerce, which were divided into (5) those with 1977 production of 1 million pounds or more, (6) those with 1977 production of less than 1 million pounds, and (7) those whose 1977 production was unknown or inaccessible because of manufacturers' claims of confidentiality. The sizes of each category in the select universe, the sample, and the subsample are presented in Figure 1.

The lists of substances making up the select universe were compiled on the basis of intended use, rather than toxicity. The intended-use theme was preserved throughout sample selection, data analysis, and inference-making, and it is reflected in the conclusions. Some structural classes of chemicals might be "overrepresented" in the subsample (e.g., cottonseed oil, linseed oil, and peanut oil). However, the Committee on Toxicity Data Elements made no attempt to define the select universe by chemical-structure classes. Rather, it relied on the probabilities inherent in small random samples to choose an appropriate number of substances from each major chemical grouping.

It is important to recognize that the subsample of 100 is drawn from the seven categories defined above and that these categories often include "inert" substances that are used to formulate "active" substances. Furthermore, these categories are not defined by chemical structure, so structurally similar substances in the subsample of 100 should not be combined for inference to the select universe. Similarly, inferences about a category should not be limited to the "active" substances in the category (e.g., drugs), but rather should be applied to all the substances (e.g., drugs and excipients in drug formulations) in that category. Nor is the subsample representative of substances involved in specially publicized episodes of toxic effect, such as those associated with thalidomide or dioxins. These kinds of substances are often selected for toxicity testing, because there is a particular interest in them--e.g., because some toxic effect has been observed. Thus, selection of substances that have already had some testing does not necessarily constitute random sampling of all possible substances in the select universe.

The Committee on Toxicity Data Elements developed a well-structured, stepwise approach to the determination of toxicity-testing needs for substances in the select universe. This required agreement on a strategy for judging the adequacy of toxicity data, establishment of guidelines for assessing the quality of individual toxicity studies, and creation of a decision-making system for reviewing and evaluating the total data base on the hazard of a substance--its toxicity, its exposure potential for humans, and its chemical and physical characteristics.

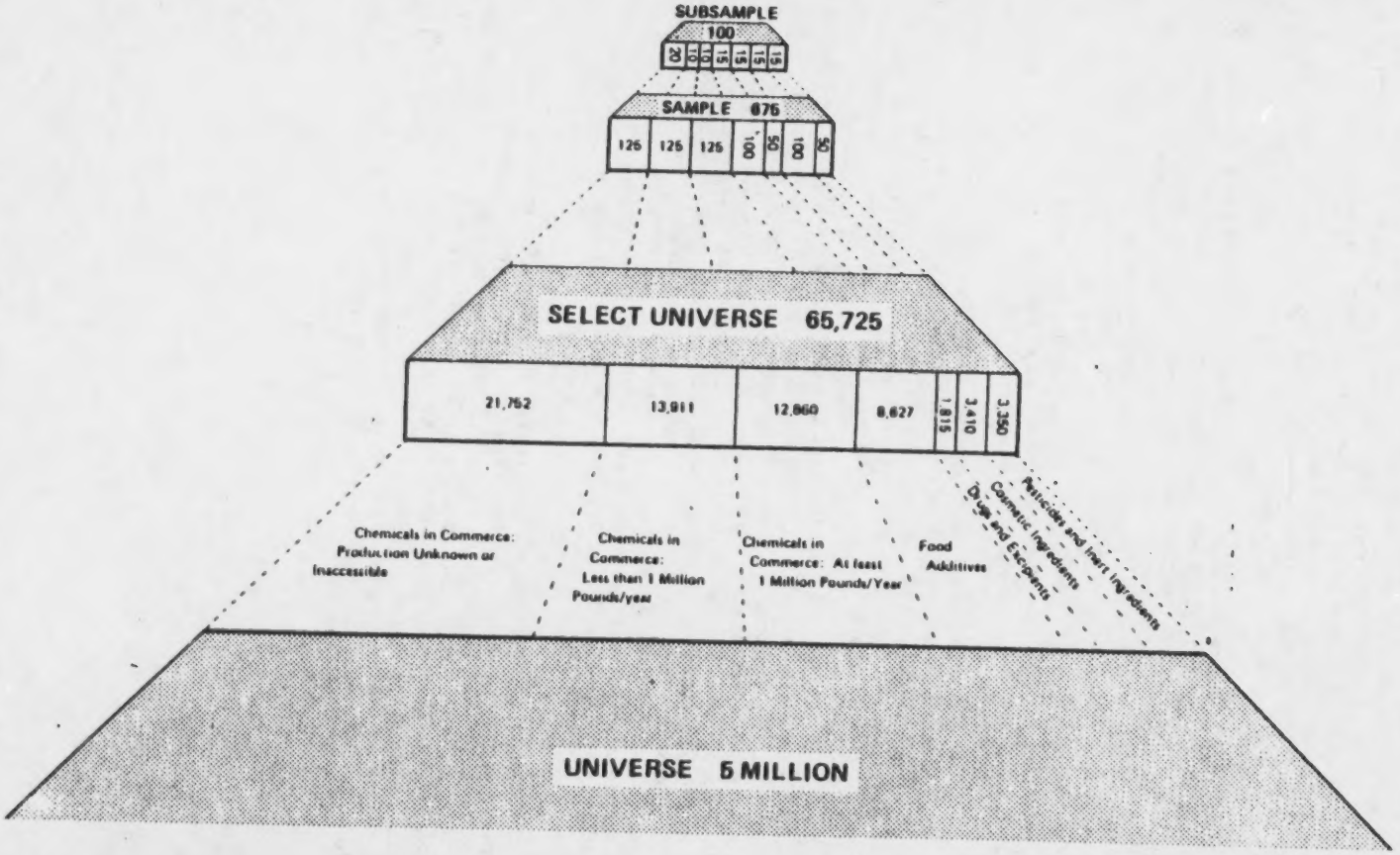

FIGURE 1 Content and size of each category in the select universe, sample, and subsample.

Results of these efforts were applied to the subsample to establish the extent of additional toxicity testing that might be needed. Data on the sample and the subsample were then used by both committees to estimate toxicity-testing needs for the entire select universe.

The Committee on Toxicity Data Elements judged the quality and completeness of the toxicity data base on each substance in the subsample. To ensure quality, available information was checked against established reference guidelines for toxicity-testing protocols (e.g., those of the Organisation for Economic Co-operation and Development) that have been widely reviewed and generally accepted. The committee also relied on the accumulated experience and expertise of its members, whose combined judgment was used to determine the adequacy of an individual study if it did not meet the standards of the reference protocol guidelines. The committee's determination of the adequacy of toxicity testing for conducting a health-hazard assessment was based on information derived from experiments performed according to the reference protocol guidelines and other information that met the committee's own basic criteria for evaluating scientific methods (described in Chapter 4 of Part 1). Using this combination, the committee assessed the adequacy of the toxicity-testing protocols and the need for further toxicity tests in detailed evaluations, tabulations, and analyses for all substances in the subsample. The committees recognize that regulatory agencies' standards and requirements for testing may differ from those used in this study.

As analysis of the data bases proceeded, the Committee on Toxicity Data Elements established a working document with a standardized format, content, and method of reporting for each of the 100 substances in the subsample as the focal point for all document control efforts and all evaluations of testing adequacy. The working document or dossier became the unit of record for all committee decisions and actions.

The approach developed to collect data on each substance included searches of open literature (primary sources) through automated, on-line data retrieval files; secondary-source literature, such as reference manuals and textbooks; government technical reports; files of U.S. regulatory agencies; and files provided by some chemical manufacturers and trade associations. The data obtained from searches of the primary and secondary open literature constituted the bulk of the information in the dossiers. Search strategies were carefully developed to ensure the most efficient screening of the data bases selected.

The findings of the Committee on Sampling Strategies and the Committee on Toxicity Data Elements are based on analyses of the sample of 675 substances randomly chosen from the select universe and the subsample of 100 randomly chosen from the sample that had at least what the latter committee defined as prescribed minimal toxicity information. Some specific analyses are derived solely from the sample or the

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subsample. Others are derived from combined information on both the sample and the subsample. Confidence limits are given for the results of analyses in Chapter 5 of Part 1. In some cases, the confidence limits are wide.

The committees recognize that, despite extensive efforts to obtain all information, they might not have had access to results of some toxicity tests. Toxicity-testing information on the subsample of 100 substances was sought from industries and other interested parties via a Federal Register notice and by direct contact with manufacturers and importers of sampled chemicals in commerce, but some industrial information probably remained unavailable to the committees. Similarly, the committees were not able to examine toxicity, physical, and chemical information on cosmetic ingredients, drugs, excipients in drug formulations, and food additives that may be in the files of FDA, except in the case of food additives listed as substances generally regarded as safe (GRAS).

The documentation for decisions about the quality of tests that have been conducted and about toxicity-testing needs lends particular strength to this study. Scientists have varied opinions about protocol guidelines for toxicity tests, about testing needs for specific uses of substances, and about grounds for claims of adequacy or inadequacy of a particular test as it was performed. Where such varied opinions are important, they can become an integral part of the decision-making process to provide new estimates of testing needs. In the context of this study, scientific judgments used by the committees were recorded and subjected to peer review in a flexible study framework that would accommodate changes in estimates brought about by the presentation of new data.

QUANTITY AND NATURE OF TESTING

It was recognized from the beginning that the quantity and nature of testing needs were such that they could never be fulfilled adequately only by the use of specific testing regimens. Although tests of substances will always be needed, a better understanding of the "how" and "why" of toxic injury itself at the subcellular, cellular, organ, and whole-animal levels will be necessary in the future to fulfill the needs in the most efficient and economical manner. The Committee on Toxicity Data Elements used a battery of toxicity tests as the basic "measuring stick" for quantitation of testing needs. At the same time, it rejected the concept that every substance in the select universe required the adequate performance of a complete battery of toxicity tests for a human-health hazard assessment, even if that were practical. Thus, other criteria, including data from human exposures, were also used for judgments about testing adequacy. The Committee on Toxicity Data Elements recognizes that meeting the testing needs will require the establishment of priorities for the tests and the substances needing them.

In the seven categories of the sample of 675 substances, testing for acute and subchronic effects was generally present more frequently than testing for chronic, mutagenic, or reproductive and developmental effects (see Table 7 in Chapter 5 of Part 1). On the basis of an analysis of the randomly selected sample of 675 substances, 75%-of the drugs and excipients in drug formulations in the select universe have at least some information on acute toxicity and 62% have information on subchronic testing. For pesticides and inert ingredients of pesticide formulations, these values are 59% and 51%, respectively. Testing was absent most frequently for substances on the TSCA list of chemicals in commerce, particularly for chronic, reproductive, and developmental effects.

More specifically, substances in the subsample of 100 were most frequently tested with acute oral rodent studies and acute parenteral studies (see Table 8 in Chapter 5 of Part 1). Except for drugs and excipients in drug formulations, the next most commonly conducted test was for genetic toxicity. Dermal and eye irritation studies had often been done with substances in the three production categories of chemicals in commerce.

QUALITY OF TESTING

The Committee on Toxicity Data Elements tabulated the quality ratings from evaluations of a total of 664 tests of the 100 substances in the subsample, without regard for either intended-use category or type of test conducted (see Appendix H of Part 1). When judged against currently accepted standards for toxicity testing, only 8% of the tests in the subsample met the standards of the reference protocol guidelines and another 19% of tests performed were judged to be adequate by the committee's standards. The percentages are based on the one study of highest quality when two or more studies of the same type were done.

The quality of design, execution, and reporting of toxicity studies was not uniform among the various types of experiments. Some test types (acute oral administration in rodents, acute dermal application, acute eye irritation and corrosivity, guinea pig skin sensitization, and subchronic dermal application for 90 days), were deemed not to require repetition in most cases where they had been conducted.

Four acute tests of substances in the select universe were often of acceptable quality: acute oral administration in rodents (83%), acute dermal application (87%), acute dermal irritation and corrosivity (81%), and acute eye irritation and corrosivity (76%). Fewer chronic test types were of acceptable quality; these included multigeneration reproduction in rodents (33%), carcinogenicity in rodents (52%), chronic toxicity (38%), and combined carcinogenicity and chronic toxicity in rodents (50%). Overall, more testing is needed for chronic toxicity than for acute toxicity. These findings should be viewed in perspective: the comparison is of simple acute tests with more complex chronic tests;

far fewer chronic tests were performed than acute tests; and, although the percentages themselves are high, they are derived, on the whole, from small numbers of evaluated tests, particularly in the case of chronic studies.

Evaluation of individual study protocols by the Committee on Toxicity Data Elements was always accompanied by documentation of the reasons for the particular ratings given to the studies. For the most part, these reasons were statements of specific adequacies or inadequacies in a testing protocol. They were collectively tabulated for analysis to assess which deficiencies were most prevalent and what values should be placed on the deficiencies when the overall value of a study was assessed.

Some of the more common deviations from reference protocol guidelines that nevertheless resulted in a test's being rated as adequate included the use of too few animals per dosage group, the use of too few or improper doses, and the absence of observations (e.g., in clinical chemistry or histopathology). In most cases, such tests were considered to have been conducted adequately because more information would not be expected to alter the conclusions, because existing data were sufficient to evaluate toxicity or calculate an acceptable LD_{50}, or because doses were high enough to give positive results or exceed the limit test prescribed in the guidelines. The Committee on Toxicity Data Elements notes that reference protocols are developed for general application before it is known which of their results will be important. The committee judged the quality of studies after they had been performed and in the light of the results obtained.

Tests that were rated as inadequately conducted often lacked required observations (e.g., test animal description, diet analysis, chemical analysis, clinical chemistry, and histopathology), used too few doses, or lacked sufficiently detailed end points, such as data tabulation and statistical analysis of data. Occasionally, the committee recommended that these studies not be repeated, either because toxicity was sufficiently well established or because more information would be of slight value.

TOXICITY-TESTING NEEDS

For pesticides and inert ingredients of pesticide formulations, the Committee on Toxicity Data Elements considered 18 test types to be necessary according to the standards it adopted. In this category, all studies of acute oral administration in rodents were judged not to require repetition. Some of the 17 remaining test types needed repetition or were not done at all from 20% to 73% of the time. For cosmetic ingredients, this ranged from 67% to 100%; for drugs and excipients in drug formulations, from 25% to 60%; for food additives, from 33% to 80%; and for chemicals in commerce, from 45% to 100%. This information indicates that, for each category of intended use, substantial testing or retesting remains to be performed for all categories of substances if information gaps are to be

filled. The major gaps in testing result from failure to do tests required by the committee according to the standards it adopted, rather than from conducting tests improperly (see Tables 12-18 in Chapter 5 of Part 1). If the unknown amount of information that was not available to the committee had been available, the "untested" category would be somewhat smaller than reported here.

In general, chronic studies, inhalation studies, and more complex studies with specific end points (e.g., neurotoxicity, genetic toxicity, and effects on the conceptus) are most frequently needed. These were among the test types considered by the Committee on Toxicity Data Elements to be necessary for conducting a health-hazard assessment according to the standards it adopted. There are some differences in the gaps in toxicity information from one category of substances to another. To some extent, these may reflect the spectrum of individual tests that the committee prescribed as necessary to meet its criteria for adequacy of information in each category.

The three greatest testing needs for health-hazard assessment of pesticides and inert ingredients of pesticide formulations were in teratology, neurobehavioral toxicity, and genetic toxicity (see Table 19 in Chapter 5 of Part 1). For cosmetic ingredients, testing was found to be needed most for subchronic eye toxicity and subchronic neurotoxicity. A large variety of test types were found to be needed for drugs and excipients in drug formulations, for food additives, and for the three production categories of chemicals in commerce.

HEALTH-HAZARD ASSESSMENT

The Committee on Toxicity Data Elements and the Committee on Sampling Strategies made judgments to describe their ability to make health-hazard assessments of substances in each of the seven categories of the select universe as complete, partial, or none. A complete health-hazard assessment was defined as one that provided a full estimate of hazard associated with the safe use of a substance. A partial health-hazard assessment was defined as one that provided a limited characterization of the hazard associated with the safe use of a substance. Therefore, a partial health-hazard assessment had a broad range extending from very limited (e.g., acute-toxicity evaluation by one route of administration) to almost complete (e.g., full acute- and chronic-toxicity evaluation, except for inadequate neurobehavioral-toxicity determination). The estimates of percentages for health-hazard assessment combine data obtained from the sample of 675 substances used to measure the existence of minimal toxicity information and the 100 with minimal toxicity information that were examined for the quality of test protocols. Results of this analysis indicate not only the percentage of substances in each of the seven categories in which sufficient data of adequate quality are available for a health-hazard assessment when judged against the current standards for protocols, but also the percentage that would require additional testing if an assessment were to be performed.

The overall status of toxicity information and of the ability to conduct a health-hazard assessment for each use category is presented in Figure 2. In general, proportionately more testing has been undertaken on pesticides and inert ingredients of pesticide formulations and on drugs and excipients in drug formulations than on other substances. In these two categories, 36% and 39% of substances met the requirements for minimal toxicity information, respectively. The Committee on Toxicity Data Elements judged it possible to make at least a partial health-hazard assessment for 94% and 92% of the substances with minimal toxicity information in each of these categories, respectively.

Cosmetic ingredients and food additives have been somewhat less well tested. Minimal toxicity information requirements were met by 26% and 20% of substances in these categories, respectively, and at least a partial health-hazard assessment was judged possible for 62% and 95% of the substances with minimal toxicity information in these categories, respectively.

In contrast, only about 20% of the substances in each of the three categories of chemicals in commerce have minimal toxicity information. In all three categories, at least a partial health-hazard assessment was possible for about half the substances having minimal toxicity information. Virtually all the substances in the three subsample categories of chemicals in commerce with minimal toxicity information would require additional toxicity testing if a complete health-hazard assessment were needed. The frequency and quality of testing of chemicals in commerce were not related to production volume. Chemicals in commerce produced in quantities of 1 million pounds or more in 1977 have not been tested more often or more adequately than those produced in smaller quantities.

INTERPRETATION OF PHYSICOCHEMICAL AND EXPOSURE DATA

The committees attempted to relate the quantity and quality of toxicity testing of each substance in the subsample to breadth of known exposure, expected trends in exposure, physicochemical properties and chemical fate of the substance, strength of evidence of toxicity in humans, and severity of reported chronic human toxicity. In addition, the committees sought information on occupational and environmental exposure and attempted to relate it to the extent of testing needs.

It became evident as the dossiers for the 100 substances in the subsample were examined that characterization of the substances with respect to each of these factors, when possible, was based on scanty information. Most of the available information was on the physicochemical properties of the substances; the least was on exposure. However, no comprehensive method of gathering the needed information could be identified, and, in the end, the principal basis for characterizing exposure was the knowledge and expertise of the committee members. The immediate use of substances in the synthesis of new substances may not result in a reduction of exposure intensity, but will reduce the number of persons exposed.

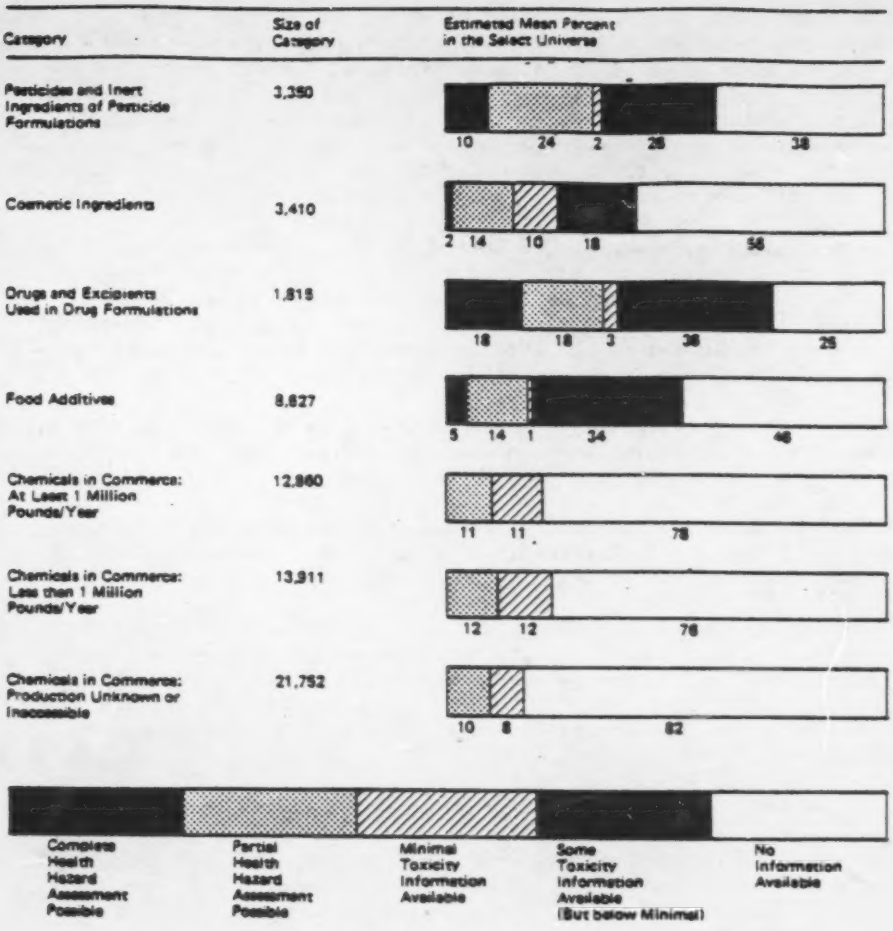

FIGURE 2 Ability to conduct health-hazard assessment of substances in seven categories of select universe.

It should be emphasized that the study was designed to characterize the status of toxicity-testing needs for substances to which there is known or anticipated exposure, without regard in the selection process to the extent of that exposure. The 100 selected substances contained, in each category, few of the substances known to be produced in the greatest volumes. Hence, this study may not provide an accurate estimate of the status of toxicity information on the principal substances to which humans are exposed.

The following observations emerge from the committees' analysis:

- Of the 100 substances in the subsample, 42 (those with at least minimal toxicity information) were considered to involve widespread exposure. An additional 14 were considered to have limited exposure potential, which would be intensive for specific groups.

- Physicochemical data on 20 of the 100 substances led to a high concern about potential adverse human health effects. For 32 additional substances, the concern was moderate.

- There was no relation between the amount of testing that had been performed and the degree of concern about a substance based on physicochemical information.

Among the seven categories, it is the chemicals in commerce that have the smallest amount of information relevant to human exposure in the workplace and in the general environment. This is of particular concern, inasmuch as the primary motivation for testing chemicals in commerce is their potential for environmental and occupational exposure.

The committees suggest that a coordinated effort be made to collect information needed to assess potential human exposure in the workplace and in the general environment. Development of analytic methods; systems for monitoring ambient air, water, soil, and foods; personal monitoring systems; and highly sensitive and selective instrumentation for the evaluation of human exposure should be integral parts of this effort.

APPROACHES TO PRIORITY-SETTING

Part 1 of this report shows that, of tens of thousands of commercially important chemicals, only a few have been subjected to extensive toxicity testing and most have scarcely been tested at all. Many other constituents of the human environment, including natural chemicals and various contaminants, are also potential

candidates for testing. Although it can be convincingly argued that many chemicals do not need to be tested, because of their low potential for human exposure or for toxic activity, it is clear that thousands or even tens of thousands of chemicals are legitimate candidates for toxicity testing related to a variety of health effects.

Many government and private institutions have responsibilities for toxicity testing, and the National Toxicology Program has a special mission to develop testing methods and to fill in the gaps left by other institutions. However, the resources available to NTP for testing--whether expressed in terms of budget, staff, or facilities--are limited. Hence it must decide which chemicals to test and which tests to perform. The need for priority-setting is especially acute for lifetime bioassays, which may cost up to a million dollars for a single chemical. Priority should presumably be assigned to chemicals and tests that are in some sense the most important. The Committee on Priority Mechanisms interpreted its charge to include defining "most important" and indicating how to identify the chemicals and tests that satisfy the definition. That is, the committee concluded that definition of the goal of the testing program was essential to designing a priority-setting system and that the goal would largely drive the logic of the design.

Testing priorities have traditionally been assigned on the basis of expert judgment, which is now supplemented with a variety of analytic, data-based techniques, such as scoring systems. The committee believes that this basic pattern should continue, with further improvement in techniques to allow expert judgment to be most effective. The committee recognized that no priority system, scheme, or procedure can be perfect, because the knowledge needed for unerring selection of the most important chemicals and tests is the same as the knowledge resulting from a complete and accurate testing program for all chemicals, which would of course make priority-setting unnecessary. The priority-setting system and the testing program form a continuum whose overall objective is to yield information of maximal value about the overall hazards of chemicals.

In examining traditional approaches, including expert judgment and mechanical priority-setting systems, the committee found some common themes that can be considered conventional wisdom and with which it agrees:

- Long lists of candidate chemicals need to be reduced to short lists through screening, which yields increasing amounts of information on decreasing numbers of chemicals and possible tests.

- The two key elements for screening are estimated human exposure and suspicion of toxic activity. (This priority-setting effort is oriented to human health and not to effects in other species, except insofar as they point toward human effects.)

- Chemicals that have already been tested adequately for a given effect are of low priority for further testing for that effect.

Although documentation on the goals of most systems is somewhat vague, all systems seem to use the goal of reducing the uncertainty about the hazards of the population of chemicals in the human environment as rapidly as possible within the limits of available resources. The key elements embodied in this goal are hazard (determined by both exposure and toxicity) and reduction of uncertainty. Testing is needed most where uncertainty is greatest; there is no need to continue testing for hazards that are already well known. The above objective not only seems to be the common denominator of current procedures for priority-setting, but is obviously a worthy goal, because it allows society the best chance to make decisions about chemicals that will reduce their hazards or at least to accept them with full knowledge of the magnitude of their hazards.

Of course, there are other legitimate goals of the testing program and therefore of priority-setting. On the one hand, general improvement in the understanding of chemical toxicity is worthy in itself; on the other, testing directed at chemicals of great public concern to confirm or deny the concern, and thus reduce anxiety, is worthy. These goals are best addressed by subjective exercise of expert judgment and were not addressed further by the Committee on Priority Mechanisms.

Given a goal for the priority-setting system, the committee needed to decide whether improvements over current procedures for selecting chemicals for testing were possible. It concluded that improvements were possible--at least at the margin--by injecting additional systematic information-gathering and -processing procedures. Many current procedures skirt the issue of the goal of the testing program and therefore are somewhat inconsistent in approaching the goal. In particular, the concept of the value of information is an important contribution to systematic priority-setting. In brief, this concept asserts that the value of any information-gathering activity, such as toxicity testing or searching for information on human exposure to chemicals, lies in the value of the resulting information in guiding decisions. The contribution of this concept is in making explicit that the goal of the testing program should be embodied in the priority-setting system.

In the realm of chemical hazards, the "cost" of not knowing the degree of toxicity of a chemical (or the degree of human exposure to it) lies in misclassifying its hazard--e.g., believing that it is innocuous, when it is actually toxic. Maximizing the value of information about chemical hazards--or, equivalently, minimizing the cost of misclassification of them--is therefore essentially the same as the goal emphasized earlier. Thus, incorporating the value-of-information concept explicitly in the priority-setting system provides an advantage, even though current procedures often use it implicitly, even if erratically.

The committee identified a second category of potentially important improvements. It includes provisions for validating some key estimates produced by the priority-setting system and thereby allowing for a self-improvement cycle to modify the system accordingly. Current systems are difficult to validate, because they rarely yield estimates that are directly verifiable, but simply indicate which chemicals to test for which effects. The committee proposes to redefine the elements of the priority-setting system to allow them to be checked. For example, an ideal system would estimate the percentage of chemicals that would yield positive results if tested; as experience accumulated, it would be possible to modify the system on the basis of the errors in the estimates. We note again that a priority-setting system cannot be free of errors in selecting chemicals for testing or in classifying them by degree of hazard when the test results are in, but any good system should reduce the frequency of errors as information accumulates and improvements become possible.

With these broad kinds of improvement in mind, the Committee on Priority Mechanisms decided to outline an illustrative system that would incorporate the stated goal and general features, building on the experience of previous priority-setting procedures, but trying to make them more systematic, defensible, and robust. The committee recognized that its own resources were inadequate to develop a fully operational priority-setting system with all the desirable features, but it hoped to provide NTP with sufficient guidance and examples to enable it to improve its current selection system while adhering to its institutional operating principles.

Several design principles became evident and were used by the committee in developing an illustrative priority-setting system:

- Any rational system can be conceptually divided into stages, with more information on fewer chemicals and fewer potential tests in each succeeding stage. The committee describes how a four-stage system might be designed. In this system, Stage 1 acts as a coarse screen and depends almost totally on automated information sources; Stage 2 begins the use of expert judgment; Stage 3 relies heavily on traditional expert judgment with only minor changes; and Stage 4 is the testing program itself.

- Both exposure and suspected toxicity considerations are useful in every stage of priority-setting. Information on either would necessarily be relatively crude (that is, there would be relatively little information about degree of hazard) at early stages, but would be correspondingly less expensive to acquire.

- Many indicators of exposure and toxicity are available--e.g., for exposure: production volume, use patterns, and persistence; for toxicity: chemical structure and the results of an acute test.

Whether or not to use a specific indicator at a particular stage of priority-setting depends on its cost, its individual value in characterizing exposure or toxicity, and its combined value with other indicators in characterizing degree of chemical hazards.

- The performance of a system should be evaluated according to its ability to characterize the hazards of groups of chemicals, not only its ability to indicate test-no test decisions.

- To accomplish test objectives, a system must take into account the frequency of occurrence of various properties (e.g., carcinogenicity) and of various indicator values (e.g., a positive result of an acute test) in groups of chemicals.

- An ideal system would be capable not only of dealing with a relatively small number of chemicals nominated to NTP by agencies--as in current practice--but also of dealing with a much larger number of chemicals in the total select universe of concern (53,500, as stated in Part 1 of this report). This capability does not necessarily imply that NTP should be the entity that operates the long-list part of the system.

- Expert judgment is essential for operation of the system beyond the earliest stage, where judgment enters into the design but not into the operation. Simply put, not enough is known about chemical hazards to specify a purely mechanical system, and humans need to integrate diverse data into judgments about the degrees of exposure and suspected toxicity. However, these judgments should be made at the lowest level of aggregation needed, because humans have difficulty in integrating information and concepts that are far outside their normal range of experience.

Beyond these broad principles, possible designs for a priority-setting system are multiple, and the specific choices for design--let alone operation--depend on expert judgments. The Committee on Priority Mechanisms offers in this report a possible design (admittedly sketchy and incapable of immediate implementation) that illustrates the key departures from current practice that seem warranted. The design may look unfamiliar, because of its description in mathematical terms, but it attempts to capture how a rational person or group would set priorities for testing if able to gather, assimilate, and integrate all the relevant pieces of information in a completely informed and objective manner.

The reasoning behind the committee's design is presented in Chapter 2 and Appendix B of Part 2. This reasoning depends in part on a "model" of the system that allowed its operation to be simulated--in highly simplified form--under a variety of assumptions. The reasoning and system simulation are complex and may well challenge the reader; however, they allowed the committee to explore the overall performance

of various possible system designs with the goal of reducing uncertainties about chemical hazards--an evaluation that has not been typical in the past.

The result of exercising the model is the simplified system description given in Chapter 3 of Part 2, in which the operation of the illustrative system is described from the viewpoint of an outside observer--what happens, but not why. Thus, Chapter 3 presents the illustrative system as a "black box," whereas Chapter 4 and Appendix B of Part 2 describe the "wiring diagram" for the interior of the box.

The committee believes that a fully developed version of the outlined system not only is a plausible extension of current practice, but also would provide some improvements over existing priority-setting procedures toward the goal defined earlier. Obviously, it might not provide improvements toward other goals, but it should not impede them. Even at the margin, the improvements would probably easily justify the costs of developing, implementing, and operating the system. However, the implementation of these concepts in the illustrative system or one of similar scope would require adjustments in the established patterns of thinking about testing priorities. Specifically, full application of the proposed analytic techniques will require that each information-gathering procedure be described quantitatively with respect to its ability to identify and to characterize potentially toxic chemicals. This requirement is not readily fulfilled in our present state of knowledge. Hence, efforts toward further quantification of the performance characteristics of toxicologic methods would be essential to full implementation of the priority-setting approach proposed herein. For this reason the approach can be pursued initially on a pilot scale, with further implementation depending on the development and availability of the necessary data. The committee believes that it should be possible to institute changes in current procedures gradually without irreversibly committing resources to the novel features of its suggestions.

Testimony before the Subcommittee on the Environment of the Senate Committee on Environment and Public Works

10 April 1984

Dr. Robert K. Tucker
Acting Director
Office of Science and Research
New Jersey Department
of Environmental Protection

Lack of adequate and accurate information regarding health effects of chemicals commonly used in our society is an outrage increasingly intolerable to our citizenry. The outstanding study on Toxicity Testing by the National Toxicology Program for the National Research Council has confirmed the fears of many of us about how little we know concerning the potential adverse effects from occupational and environmental exposure to hazardous chemicals. New Jersey's recent experience with passage of its Right to Know legislation has highlighted the political potency of a public determined to gain information relevant to assessing risks to its well being. And, although I may be most familiar with details of New Jersey's experience, my meeting and working in common with health and environmental officials from other states through the National Governors' Association Toxics Integration Program, has made me aware of how widespread concern regarding hazardous chemicals is in our country today. The N.G.A. Toxics Integration Program as well as research grants to the states have been funded under provisions in the Toxics Substances Control Act (TSCA) and these grant programs certainly represent benefits from secondary sections of this substantial legislation. However, in my opinion, the much greater benefits promised from the primary legislative intent of TSCA have yet to be delivered. The chemical industry has succeeded in tying the U.S. Environmental Protection Agency in knots over confidentiality provisions and EPA seems to have choked on the

sheer volume of required information to be processed under the act. Yet TSCA, if it works, could certainly be one vehicle for changing the sorry statistics found in the National Research Council Study.

Two improvements, especially, are needed to make TSCA effective: First, the Act must be strengthened to require industry to carry out, in a timely fashion, tests necessary to determine health hazards, if such tests are lacking or are inadequate, and to furnish all relevant test data to EPA. Second, toxicity information must not be cloaked in secrecy to such an extent that it cannot be adequately evaluated or is unavailable or unusable by those who must have it to protect public health. Those of us at the state level, in Departments of Health, Environmental Protection, Environmental Conservation, or other agencies, find ourselves in the "front lines"; we must often act to protect public health in crises situations as well as in the implementation of pollution abatement programs over the long haul. The very least, needed to increase the effectiveness of TSCA, is to amend the Act to provide access for state officials to toxicity data presently restricted under confidentiality provisions. Perhaps Congress will require certain safeguards for this access, although I personally do not believe there can be any justification for holding secret information about the toxic properties of chemicals to which the public may be exposed. Restricted access to toxicity information by unreasonable

requirements to protect "confidential business information" is intolerable in the face of potential threats to health and the public welfare. If, under our Bill of Rights, the fifth amendment requirement that private property not be taken without just compensation is held to apply to test data then let provisions be worked out whereby the costs for intellectual property represented by test data on a particular chemical are shared by all those companies who stand to benefit from production, use or sales of that compound. Just compensation, not secrecy, is the answer in this instance, for those who would uphold the Constitution.

Perhaps by giving you more detail from the state perspective, I can elaborate on the necessity for amending TSCA to provide for the two improvements--more adequate data on toxicity and access to such data by the states. In New Jersey the Department of Health has responsibility for provisions regarding work place exposure to chemicals under our Right to Know legislation whereas the Department of Environmental Protection, for which I work, must implement provisions regarding community and environmental chemical exposure. Over the past few months both departments have been working closely together with County and local health departments to make sure this legislation will work to the benefit of our citizens. I've appended a synopsis of the Act prepared by the New Jersey Office of Legislative Services. The Act is fairly comprehensive in its requirement for information

about names of chemicals to which workers might be exposed or which may be emitted into the environment. Merely knowing the identity of the compounds, however, neither satisfies the intent of the Act nor the real need for public health protection. Toxicity data on the chemicals is needed in addition. The National Toxicology Program Study has done a real service in giving direction for methodology for obtaining the needed data. Congressional amendment to TSCA may insure that chemicals are evaluated and data is produced.

In addition to Right to Know, New Jersey has recently passed legislation mandating extensive testing of drinking water supplies and the setting of Maximum Contaminant Levels (MCLS) for exposure to chemicals found therein. We need toxicity information in order to properly set MCLS. For our on-going enforcement of water and air pollution regulations, for cleanup of Superfund sites, and for determination of sites for hazardous waste treatment, toxicity information is vital also. All these programs depend on accurate knowledge of toxicity of the chemicals involved; Congress can render distinct service to public health by amending TSCA to help ensure that toxicity information becomes available.

TESTIMONY

before

Subcommittee on Toxic Substances

Committee on Environment and Public Works

U.S. Senate

April 10, 1984

by

Roger A. Kanerva, Manager

Environmental Programs

Illinois Environmental Protection Agency

2200 Churchill Road

Springfield, Illinois

217/785-5735

I thank the Subcommittee for scheduling this hearing to receive testimony for the purpose of considering the status of program efforts to control toxic substances. My testimony is presented on behalf of the Illinois Environmental Protection Agency (Illinois EPA) and the State of Illinois. The Illinois EPA is responsible for administering the State's pollution control laws and regulations, and for working cooperatively

with USEPA in implementing similar federal programs. My current assignment with the Illinois EPA is to manage all media environmental programs, such as water, air and land pollution control and public water supplies plus several support functions such as laboratories and data processing.

Prior to this current assignment, I was the Manager of the Division of Water Pollution Control (DWPC) for the Illinois EPA from June, 1978 to May, 1981. Prior to that time, I worked for nearly nine years with the Water Resources Administration of the Maryland Department of Natural Resources in various program management and technical capacities. I have both B.S. and M.S. degrees in Watershed Management from the University of Arizona. I continued my education at Johns Hopkins University under their M.L.A. degree program with major emphasis on environmental and social sciences.

INTRODUCTION

In Illinois, we have made significant strides in improving environmental quality under a variety of state and federal laws. We have worked to prudently build the federal/state partnership for environmental protection in Illinois. We maintain a strong belief in the value of state management of the day-to-day operations of the national programs for air, land, and water pollution control and public water supply.

I am here today, however, to report about some very troublesome times I forsee ahead regarding adequate control of toxic chemical substances. The current regulatory system has served us well for "traditional" issues of pollution control. But can this system fully deliver what the public wants today in terms of environmental protection: assurance that it is

"safe" from toxic chemical substances?" This testimony will provide documentation, with respect to Illinois, that confirms a number of unsatisfied needs with respect to this very challenging question.

TOXICS IN ILLINOIS

Based upon data collected in 1977 for the national TSCA inventory, Illinois ranks fifth among the states in annual production of chemicals. In fact, USEPA has estimated that production of chemicals in Illinois may be as high as 129 trillion pounds. About 350 sites in Illinois import or manufacture 3,637 chemical substances according to the TSCA inventory. The Illinois EPA remains concerned, however, that current data on production and types of chemicals are not available for comparison with current data from the programs the Agency operates.

Furthermore, the inventory does not identify these chemical substances as being toxic or non-toxic. We must conclude, however, that chemicals, which could be of concern in Illinois, are quite diverse and undoubtedly include substances which may cause acute or chronic toxicity depending upon the nature of the substance, the amounts, and the type of exposure.

Once generated or transported into the State, chemical substances may become a toxics problem in a number of ways including exposure of workers, uncontrolled spills or emergency events and "controlled" releases to the environment. The following listing summarizes some pertinent data relating to principal avenues for exposure within the purview of the Illinois EPA:

- From 1978 through 1982, some 4,000 emergency incidents took place involving 165 different chemicals. The resultant impacts included 39 fatalities, 823 injuries, and 18,649 citizen evacuations. In responding to these incidents, the Illinois EPA and other agencies often face very complex and difficult decisions regarding adequate control of toxics.

- Over 500 potential hazardous waste problem sites have been identified in Illinois. Data from preliminary studies indicate that over 68,200 people live or work within a one mile radius of just 22 of these sites. Under both the Superfund and State cleanup programs, we face a myriad of future questions about "how clean is clean" regarding remedial action at these sites.

- New annual reporting requirements show that, in 1982, 616 million gallons of hazardous wastes were generated in Illinois by some 2,500 facilities. Of this amount, about 31 million gallons were landfilled, 10.5 million gallons were incinerated and about 461 million gallons were treated.

- Emissions of hydrocarbons and particulates from some 9,929 facilities in Illinois have been reduced to just 377,000 tons per year. However, available data is inadequate to define the extent of toxic chemical substances which may be of concern relating to these emissions.

- Toxic chemical substances have been found in several public water supplies in Illinois. In one instance, the presence of high levels of volatile organic solvents forced the shutdown of a municipal well. In another instance, special aeration procedures have been used to reduce the level of volatile organic compounds.

- Discharges of suspended solids from some 2,315 facilities with NPDES permits in Illinois have been reduced to about 102,000 tons per year. But not enough is known, as yet, about the chronic impacts of continued release of specific chemical substances and complex mixtures of substances.

Fortunately, the current regulatory system does provide a baseline of protection which includes both direct and indirect effects on controlling toxic substances. However, achievement of "chemical safety" will surely entail another round of specialized and intensive effort to address the more subtle impacts of chronic toxicity problems.

THE RACE TO KNOW

Scientific capability for the detection of chemical substances in the environment has advanced tremendously over the past decade. As environmental practitioners, we used to talk routinely about parts per million just a few years ago. Today, parts per billion are the common denominator in many instances, and in a few instances even more minute amounts. At these incredibly small levels, we seem to be rapidly approaching a scenario where nearly anything can be found anywhere so to speak.

In Illinois, we have found and are dealing with our fair share of "toxic hot spots." An equally challenging problem stems from the identification of "toxic cool spots" where residual levels of chemical substances are so small that any risk of significant harm is practically negligible. But if citizen emotions are running high, then any rational consideration of these risks becomes unworkable. Such showdowns are not fairly representative of the constant ebb and flow of acceptable risks that citizens effectively cope with in daily life in our modern society.

Such events have had a dramatic impact on the public. Fueled by such things as media coverage and controversy over siting of new landfills and cleanup of old problem sites, public awareness about "toxics" has skyrocketed. Concurrent with this new awareness, the public's desire for detailed analytical information about the chemical substances that could be present in the air, waterways, soil or drinking water of communities in Illinois has become a priority concern for the State program. We have struggled, with some success, to keep up with this explosion of demand

for data. State-of-the-art production equipment has enabled us to keep pace with metals testing. But even with new GC/MS equipment, we have fallen behind in testing for organic chemicals. Additional analytical equipment will be ordered in the near future which should help significantly. During FY 83, our lab performed 467,676 inorganic analyses and 63,393 organic analyses.

Legislative reactions regarding these matters have become very intense as well. Both worker and community "right-to-know" bills were introduced last year. The worker bill, "the Toxic Substances Disclosure to Employees Act of 1983," was enacted and is currently being placed into operation. This Act mandates thousands of businesses in Illinois to meet new responsibilities for worker protection with respect to some 795 listed chemical substances.

The community bill was carried over to the legislative session this year. The debate regarding this initiative is just now getting underway. One proposal calls for annual reporting for nearly 1,900 chemical substances to be included in the scope of this program. Other concepts being considered include the establishment of a "toxic substances clearing house" at the State level, and the development of a "toxic substances handbook" for public distribution. These later items are reflections of the major inherent weakness which pervades all this shotgun reaction to toxics. How is the system going to be able to adequately respond to public inquiry about the potential adverse effects of all these substances? In other words, what is the practical meaning of all this blizzard of information about toxics for the citizens, businesses, and public officials of Illinois and elsewhere?

THE NEED TO UNDERSTAND

Several years ago, the Illinois EPA recognized that the State must enhance its ability to determine the relative safety of toxic chemical substances under a myriad of possible environmental and exposure settings. Furthermore, we realized that such efforts would most likely cut across traditional program boundaries within our agency and extend outside this bureaucratic realm to other state agencies such as public health and agriculture. We organized an initiative by establishing an internal Toxics Project Team and a companion external group, a Toxics Advisory Committee. These groups carried on their activities in a parallel but interactive fashion for about two years. The product of these extensive efforts, titled CHEMICAL SAFETY: An Agenda for Continued Progress in the Control of Toxic Pollutants, was published in February, 1984 and is included as part of this testimony.

This Agenda presents a blueprint or strategy for achieving a better understanding about the environmental and public health impacts of toxic chemical substances, and, eventually, enhanced control procedures. The basic building blocks of the program are identified as follows:

- Biological toxicity assessments -- Evaluation of the potential impacts of toxic pollutants should include an effective combination of chemical and biological testing procedures.
- Site-specific problem evaluations -- Toxicity problems are likely to vary widely by facility and location. Thus, data-gathering and the development of control strategies should often focus on specific sites.
- Risk management techniques -- Acceptable methods should be utilized to relate the existence of toxicity to populations at risk.

- Phased implementation -- The program should be implemented in orderly stages to ensure that new control requirements are based upon adequate monitoring of potential toxicity effects at individual facilities or within specific geographic areas, and to provide reasonable time for achieving compliance.

- Integrated management -- Current state and federal programs for air, land and water pollution control are designed to operate independently of one another. Strong state management will be necessary to ensure that toxicity problems are not overlooked or compounded because of conflicting or inconsistent requirements in individual programs.

Without question, the Agenda sets forth a very ambitious and demanding undertaking. Nevertheless, the journey must begin if we are to have any reasonable hope of effectively coping with this problem. In recognition of this need, Governor James Thompson announced the creation of the "Chemical Safety Research Center" in his State of the State message on February 8, 1984. This new Center will be jointly managed by the Illinois EPA and the Illinois Department of Energy and Natural Resources. In his proposed budget for FY 85, Governor Thompson included funds for both agencies to start-up the Center. The Illinois EPA portion of the Center involves $650,000 for the establishment of an environmental toxicity testing capability. Both central laboratory and mobile field units are envisioned as part of this program. A wide range of testing capability is planned, including acute and chronic aquatic toxicity tests, Ames bacterial analysis, Microtox bacterial analysis, and mammalian tissue culture analysis.

These new efforts in Illinois appear to be particularly timely given the status of related events at the national level. The National Academy of Sciences recently published a report titled Toxicity Testing: Strategies to Determine Needs and Priorities. This review, which was

done for the National Toxicology Program, documents a significant shortfall in the national arena with respect to the development of an adequate data base for toxic impacts of chemical substances.

This represents perplexing news from a state perspective for several reasons. Given the incredible magnitude of the toxicity testing job to be done, no single state, Illinois included, is ever likely to be able to bring enough resources together to adequately address all the chemical substances of potential concern. Thus, we must look for support and assistance from the national testing program to augment our toxics data base needs. By carefully prioritizing and targeting our toxicity testing activities, we can make significant progress at the state level to address site-specific, real-time toxicity problems. But without similar productive efforts at the national level for new and existing chemicals, we would appear to be caught in an endless loop of always being one step behind the next round of problems. Finally, Illinois wants to avoid, where possible, wasting valuable testing resources by "recreating the wheel" as compared to using information available from the national level for all states.

Failure to satisfy these state and federal data base needs for toxics control will erode public confidence in government's capability to provide adequate protection. Such loss of confidence will further exacerbate the trial by press method of creating "politically outcast chemical substances." Neither Illinois nor the rest of this country can afford to create more chemical graveyards or process toxic torts fashioned from knee-jerk or fear-ladden reactions. The upfront investment in assessment of potential toxicity problems surely represents a better strategy for cost-effective allocation of public and private resources.

THE CHALLENGE OF GOOD GOVERNMENT

The Chemical Safety Agenda has also served to focus attention in Illinois upon the pressing need for more technical expertise and better integration of program activities to achieve improved toxicity control. We have documented the fact that problems with toxic chemical substances often transcend traditional program boundaries for environmental protection, public health, worker safety and consumer protection. Our experiences with handling environmental emergencies, permitting of complex, multimedia industrial facilities, remedial actions for hazardous waste sites, establishment of suitable performance standards for toxics control, and collection of ambient monitoring data for specific chemical substances all serve to reinforce the demand for "good government" to combat toxicants.

We intensified our efforts to address this need in 1983 by establishing the Office of Chemical Safety within the Illinois EPA. This Office was created as part of a package of initiatives relating to hazardous waste control sponsored by Governor Thompson. The General Assembly of Illinois was also very supportive of these efforts and approved the funding necessary for staffing this new Office. This Office has umbrella-like responsibilities for toxics control across all programs operated by the Illinois EPA. We have hired highly qualified staff with expertise in environmental science, environmental toxicology, industrial hygiene and environmental epidemeology. Under my general direction, these staff will serve as both a central point for policy and technical development and as a source of expert assistance for the line programs.

This Office will also perform a lead role in managing special projects to assess "toxic hot spots" in Illinois. For example, we are currently completing the first phase of a special study of a twenty-five mile square area in South Chicago. This study was initiated by the Illinois EPA in response to intense local concerns about the extent of hazardous waste landfilling in this area. While landfilling started-out as the principal concern of several citizen groups, subsequent dialogue and field visits rapidly expanded the scope of the project into an air, land, and water matter. Along with this expanded scope, came the need for a team approach among the Illinois EPA, the Illinois Departments of Public Health and Energy and Natural Resources, and Region V, USEPA.

One especially innovative feature of this study involved a contract for air toxics monitoring using a mobile van containing GC/MS analytical and computer equipment. This highly sophisticated field tool had never been used in Illinois before this study. This developmental effort may serve as a foundation for future State capability along these lines.

We have been successful in documenting the existence and areal nature of a number of organic and inorganic substances as part of this study. We also feel confident that no severe, acute toxics problems are at large in the study area. What remains most elusive at this point, however, are the long-term chronic impacts of all these substances. The available health data does not show any alarming trends, but cannot conclusively answer the chronic concerns. Thus, we anticipate a second phase to this study wherein toxicity testing and multimedia modeling techniques will be used to enhance our understanding of the potential for adverse effects from toxic chemical substances. This second phase can also serve as a

continuing vehicle for improving the team approach among the many agencies involved.

While we have made significant progress to address the "good government" issue in Illinois, we cannot operate in a vacuum regarding toxics control. Activities at the federal level of government certainly play a major role as well. In the Chemical Safety Agenda, we identify some serious concerns regarding the interrelationships among the many federal programs affecting toxic substances control. In particular, we emphasize the neglected opportunity for better use of TSCA as an umbrella mechanism for integration and coordination of toxic control activities. TSCA could serve as a powerful tool for buttressing the information weaknesses of other environmental management programs.

From a state perspective, however, TSCA currently leaves something to be desired with respect to a sound federal/state partnership. States are excluded from access to confidential information about some toxic substances even though they may be wrestling with similar matters on the home front. This is especially frustrating in light of state level guards for confidentiality such as are in effect in Illinois.

TSCA has also been implemented in a manner which leaves the states as a largely untapped resource. To my knowledge, only five states have been granted funds under cooperative enforcement agreements with the USEPA. This seems especially awkward given the exact opposite approach utilized for the air, water, land and drinking water programs. In Illinois alone, there are over 2,000 facilities subject to federal PCB regulations which could be more efficiently and effectively monitored at the state level for a very modest investment by the USEPA.

Along these same lines, Section 28 of TSCA has not developed into a national management tool for helping states to implement more integrated, multimedia strategies for control of toxic substances. Only seven states have ever received federal grants under Section 28 for special projects relating to toxics control. I would like to suggest that Section 28 could be viewed as a continuing mechanism for providing cooperative program grants to the states for enhanced control of toxic chemical substances.

CONCLUSION

State environmental and public health programs must assertively address the growing public concern regarding "safe" control of toxic chemical substances. We cannot coast along based on past progress. Rather, we must gather new kinds of data, implement new assessment techniques and design better controls, where needed, all in a timely manner. This must, of course, be done within prudent fiscal constraints which impact both state and federal government.

The troublesome times I foresee could be greatly aggravated if government fails to exercise the leadership necessary to get its act together on toxics control. On the one hand, most of the major regulatory tools for corralling toxics appear to be readily available. On the other hand, there certainly appears to be a justifiable need for some fine-tuning of these tools and of the manner in which they are utilized. But do we have the will to resolve these matters before the toxics pot boils over? This question I leave to the Subcommittee in whose hands the making of national policy must rest.

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CHEMICAL SAFETY:

An Agenda for Continued Progress in the Control of Toxic Pollutants

ILLINOIS
ENVIRONMENTAL PROTECTION AGENCY

February, 1984

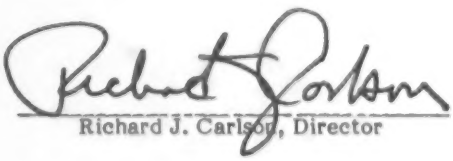
[The following has been excerpted from the above named report. The complete report has been retained in committee files.]

PREFACE

The Illinois EPA is pleased to present this strategy. This effort represents the culmination of many years of activity relating to control of toxic pollutants.

This strategy is based on a belief that we can and must do an effective job of controlling toxic pollutants in Illinois. While we recognize that much progress has been made, we must re-dedicate ourselves to the vital task of protecting the environment and citizens of Illinois from the adverse impacts associated with toxic pollutants.

As Director, I endorse this strategy and express my sincere gratitude to the members of the Toxics Advisory Committee and the Agency Project Team who were instrumental in the creative effort to develop this Strategy. This document represents the Agency's position on toxics control and should not be construed as an expression of consensus by the members of the Advisory Committee.



Richard J. Carlson, Director

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STRATEGY OVERVIEW

In Illinois, we have made significant strides in improving environmental quality under a variety of State and federal laws. This strategy is predicated upon these programs being fully operational such that a baseline of protection is available to build upon. These programs have developed at different times and rates over the years to address specific public health and environmental problems. The state of our scientific and technical knowledge has also been rapidly evolving so as to greatly influence our understanding of the nature of these problems.

As a result, we now find ourselves trying to cope with a complex, oftentimes fragmented and soon to be outmoded regulatory system. This system may be adequate to address "traditional" issues of pollution control, but cannot fully deliver what the public wants today in terms of environmental protection: assurance that it is safe from toxic chemical substances.

Program Status

Current environmental programs provide a substantial baseline of protection largely through technology-based controls and standards for a few dozen specific substances. The traditional approach has been to ensure that industry installs equipment that represents the "best technology" to control the most obvious sources of air, water and land pollution. These controls have focused mainly on pollutant measures which are broad indicators for the dozens or even hundreds of individual chemical compounds which may be present. With rare exception, proper implementation of these requirements controls pollutants such that immediate and severe damage is eliminated. What is much less certain, however, is the nature

of long-term, chronic impacts from exposure to residual amounts of specific chemical substances that may be toxic under certain conditions. Of course, confirming the mere presence of such substances with chemical testing often does not automatically substantiate a toxics problem, and may even waste valuable funds if testing is done just for the sake of testing. In many cases, biological monitoring and testing procedures will be necessary to adequately define and eventually regulate these problems in a cost-effective manner. In other words, toxics problems often involve a complex interplay of concern about the inherent toxicity of chemical substances and the risk that significant exposure may occur, both of which combine to influence the hazard potential.

The current approach to environmental regulation must be expanded to more effectively address the potential impacts of the many thousands of chemical substances which may still pose a significant risk to public health and the environment. Further, we know we must proceed in a manner which will serve to better interrelate and integrate program acitvities in order to address the control of toxics in the broadest possible sense.

An Agenda for Progress

Providing safety from toxic chemical substances is not possible without developing an understanding of what this really means in practical terms. This need is best satisfied by refined program requirements which serve to eliminate unreasonable risk of adverse effects on human health and the environment from exposure to toxic pollutants. The following features should serve as the basic building blocks of the program:

- Biological toxicity assessments — Evaluation of the potential impacts of toxic pollutants should include an effective combination of chemical and biological testing procedures.

- Site-specific problem evaluations — Toxicity problems are likely to vary widely by facility and location. Thus, data-gathering and the development of control strategies should often focus on specific sites.

- Risk management techniques — Acceptable methods should be utilized to relate the existence of toxicity to populations at risk.

- Phased implementation — The program should be implemented in orderly stages to ensure that new control requirements are based upon adequate monitoring of potential toxicity effects at individual facilities or within specific geographic areas, and to provide reasonable time for achieving compliance.

- Integrated management -- Current state and federal programs for air, land and water pollution control are designed to operate independently of one another. Strong state management will be necessary to ensure that toxicity problems are not overlooked or compounded because of conflicting or inconsistent requirements in individual programs.

Conclusion

As with any planning process, part of the value obtained results from the pursuit of the process itself. Making the effort to reach out beyond everyday program concerns has brought new insights about current activities and new visions for future program directions. Many external factors will affect the degree to which a toxics control strategy can be implemented. But without a coherent beginning, we risk making no progress at all.

TOXICS IN ILLINOIS

Illinois is fortunate to be blessed with a rich mixture of natural resources that help sustain a large and diverse economy. However, the State faces a dilemma common to other industrialized states; that is, reaping the economic benefits of manufacturing and using chemical substances while at the same time controlling adverse impacts caused by some of these substances.

Under the auspices of the Toxic Substances Control Act (TSCA), the USEPA developed and maintains an inventory of chemical substances involved in commerce in the United States. About 58,000 chemicals are now listed on this inventory based upon data collected in 1977. About 350 sites in Illinois import or manufacture 3,637 chemical substances contained on the TSCA inventory. These sites reported their annual production of chemicals in ten categories ranging from under 1,000 pounds to over 1,000,000 pounds. By aggregating these data, USEPA has estimated that production of chemicals in Illinois may be as high as 129 trillion pounds. These levels place Illinois fifth among the states in annual production of chemicals. These chemicals, however, are not identified by the inventory as being toxic or non-toxic. Thus, we can only state that the origin and kinds of chemical substances which could be of concern in Illinois are quite variable and undoubtedly include substances which may cause acute or chronic toxicity depending on the nature of the substance(s), the amounts, and the type of exposure. The Illinois EPA remains concerned, however, that current data on production and types of chemicals are not available for comparison with current data from the programs the Agency operates.

Once generated or transported into the State, chemical substances may become a toxics problem in a number of ways. Exposure of workers is one avenue for adverse impacts to occur. This strategy assumes that the "Toxic Substances Disclosure to Employees Act" recently enacted in Illinois will address this matter. Sudden, uncontrolled spills from accidents and other emergency events, and controlled releases to the environment are the other principal avenues of exposure within the purview of the Illinois EPA.

From 1978 through 1982, there were 4,000 emergency incidents involving about 165 different chemicals resulting in 39 fatalities, 823 injuries requiring hospital examination or admittances and 18,649 citizen evacuations. In the past twenty years, over 12,800,000 fish have been killed by pesticides and other wastes discharged into the waterways of the State. The largest fish kill ever documented in the State occurred in 1982 and was attributed to a spill of nitrogen fertilizer solution which affected nearly 30 miles of stream and destroyed some 418,000 fish. Thus, commercial agriculture can be a significant source of toxic pollutants. Pesticide residuals are found in air, water and soils as the result of crop protection chemicals being applied on over 23 million acres of farmland in Illinois each year. In 1982, 65.4 million pounds of herbicides, 7.3 million pounds of insecticides and 1.0 million pounds of nematocides/fungicides were used to guard against competitive weeds and destructive organisms in Illinois. Agrichemical storage and waste management practices are additional concerns related to agricultural production. Despite the current trend toward handling chemicals in larger, re-usable, containers over 600,000 pesticide cans must be disposed of annually in Illinois.

Among the environmental management programs, the land pollution control program (hazardous and solid wastes) is the most recent activity to receive significant attention by the state and federal government. This latest challenge involves both cleanup operations to correct past abuses and implementation of new control programs to prevent future problems. As early as 1979, the Illinois EPA conducted a survey to characterize the general magnitude of the process wastes resulting from the industrial activities of 20,981 facilities in the State. The annual quantities of process wastes were estimated to be 14 million tons and 1.5 billion gallons of materials. The industrial categories which were major contributors included electric and gas services, iron and steel manufacturing, inorganic chemicals, miscellaneous chemicals, machine and mechanical products, electroplating and coal mining.

The USEPA, with assistance from the states, has developed a national inventory of potential hazardous waste problem sites. Over 500 such sites are listed for Illinois. The Illinois EPA is currently in the process of conducting preliminary assessments and, if necessary, site investigations for each of these sites. In addition, the Agency has already completed studies of 27 high priority sites, 11 of which have been included on the National Priority List for the national Superfund program. Data from these studies indicate that over 88,200 people in Illinois live or work within a one mile radius of 22 of these sites. Under the federal hazard ranking system, these data serve as an indicator of the possible risk to the public. Funding from both the Superfund and State Hazardous Waste Fund is targeted for undertaking the necessary remedial cleanup actions which have been estimated to cost over $100 million for the 27 sites alone.

In addition to this cleanup operation, the Illinois EPA must, of course, address the safe handling of hazardous wastes being produced today. This has proven to be especially challenging given the relatively late arrival (1980-82) of federal requirements for hazardous waste control as compared to the other environmental regulatory programs (1972-77). New annual reporting requirements show that in 1982, 623 million gallons of hazardous wastes were generated by 2,500 generators and treated, stored and disposed of by 350 facilities in Illinois. Of the 623 million gallons of hazardous wastes, 557 million gallons were managed on-site and 66 million gallons were handled off-site in Illinois. Deep well injection accounted for a significant portion of the total on-site amount.

A major change in waste disposal practices began in late 1980 with the initial implementation of the federal Resource Conservation and Recovery Act. Waste generators began to move away from landfilling to an increased reliance on treatment and recycling. In 1980, 94,860,000 gallons were landfilled at off-site facilities. In 1982 only 34,600,000 gallons were landfilled. Incineration increased from 64,000 gallons in 1980 to 2,200,000 gallons in 1982. Treatment increased from 3,377,000 gallons in 1980 to 15,700,000 gallons in 1982. Data collected early in 1983 indicate a continued rise in recycling and recovery as well. These increases in incinceration and treatment, however, indicate possible important impacts in the air and water programs which must be carefully managed to prevent the transfer of adverse impacts.

Some chemical substances are allowed to be released into the air or water following treatment pursuant to federal and state environmental laws and regulations. For the most part, these programs have served to correct or prevent acute health or environmental problems. Of continued concern, however, are

chemical substances that may cause chronic toxicity problems such as cancers, birth defects, sterility, genetic mutations, neurotoxicity, organ damage, immunotoxicity and bioaccumulation in the environment. The emissions of hydrocarbons and particulates from some 9,929 facilities in Illinois, which have air pollution control permits, have been reduced to just 377,000 tons per year. However, there is, as yet, a largely undefined potential for these emissions to include toxic chemical substances of concern in particular settings. The discharges of suspended solids from some 2,315 facilities with NPDES permits have been reduced to about 102,000 tons per year. In general, industrial facilities have complied with new control requirements at a faster pace than municipal facilities. Monitoring of these discharges and related receiving waters shows that most obvious problems have been or soon will be eliminated. But not enough is known, as yet, about the more subtle, long-term impacts of specific chemical substances (particularly organic compounds) and complex mixtures of substances.

Appendix A presents a more detailed summary of the scope and magnitude of the toxics control problem for all the environmental programs. The programs and activities of the last decade are highlighted, particularly with respect to the direct or indirect effect on controlling toxic substances. While there is adequate justification for moving ahead on controlling toxics, we are not alarmist about the current situation given the significant degree of protection largely in place. Rather there is a need for a carefully developed and practical program directed towards the achievement of "chemical safety."

CHEMICAL SUBSTANCE USE

Chemical Manufacturing and Use

The Toxic Substances Control Act (TSCA) was enacted by Congress in 1976 to control all potentially harmful chemicals and uses not already covered by other legislation. Drugs, foods, pesticides, substances in consumer products, occupational hazards and general pollutants are mostly or partly covered by a number of other laws. TSCA is meant to assess and protect against the risk to the environment and humans from new chemicals as well as improving control of substances already in production and use where necessary. TSCA provides much insight into the nature of legislative intent regarding regulation of toxic chemical substances. TSCA was clearly meant to be the umbrella mechanism for dealing with the safe use and disposal of chemical substances, particularly when other federal laws are inadequate to do so. As such, TSCA can be viewed as setting the overall tone and direction of the federal effort to control such substances.

TSCA involves substances which ... "may present an unreasonable risk of injury to health or the environment." According to a House Commerce Committee Report (Special Monograph Report, March 11, 1977, the BNA Environment Reporter):

> The standard for defining the regulatory authority of the Administrator throughout the Act is "unreasonable risk." The Committee has limited the Administrator to taking action only against unreasonable risks because to do otherwise assumes that a risk-free society is attainable, an assumption that the committee does not make.

The Reporter goes on to provide more instructive background on the intent of Congress by stating that "... the Act does not define what is an unreasonable risk, but its clear intent is that a balancing approach be used in determining what

constitutes an unreasonable risk." The House Commerce Committee Report further explains the type of balancing involved in a determination that there is unreasonable risk as follows:

> In general, a determination that a risk associated with a chemical substance or mixture is reasonable involves balancing the probability that harm will occur and the magnitude and severity of that harm against the effect of proposed regulatory action on the availability to society of the benefits of the substance or mixture, taking into account the availability of substitutes for the substance or mixture which do not require regulation, and other adverse effects which such proposed action may have on society.
>
> The balancing process described above does not require a formal benefit-cost analysis under which a monetary value is assigned to the risks associated with a substance and to the cost to society of proposed regulatory action on the availability of such benefits. Because a monetary value often cannot be assigned to benefit or cost, such an analysis would not be very useful.

For the purposes of this chemical safety program in Illinois, we must recognize that new chemical substances may be used in commerce based upon this "unreasonable risk" test. But TSCA goes even further to frame the policy context of the regulation of toxic chemical substances. Existing chemical substances which are already in use (prime candidates for release as toxic pollutants) may fall under the control of TSCA if other federal laws do not operate such that "... a risk to health or the environment associated with a chemical substance or mixture could be eliminated or reduced to a sufficient extent ...". This standard for existing chemicals presents another policy imperative about the relevance of risk analysis and the overall focus upon minimizing such risks. Furthermore, this standard also raises some interesting questions relative to the policy and legal structure of the other major environmental laws.

The USEPA is the designated agency to administer TSCA. There are no delegated state responsibilities comparable to other federal environmental laws. Indeed, the Act even preempts state regulation of substances subject to USEPA control. However, the Act allows grants to states for specific problems relating to toxics identification and control. The Illinois Department of Public Health received one of these grants to assist in the development of an environmental toxicology program. While is is clear that TSCA should continue to be a national program, increased participation by the states could prove beneficial. At a minimum, the Illinois EPA needs to upgrade efforts to track and evaluate TSCA activities as they affect control of chemical use in Illinois. This is especially important in light of recent Congressional concern about the adequacy of implementation of TSCA by USEPA.

Wastes Viewed As Resources

A major purpose of TSCA is to prevent the introduction of toxic chemicals for uses that could expose the public to unreasonable risks. Another preventive approach is greater recognition of "wastes" as potential resources. Conservation, recovery and recycling can be useful techniques for reducing the amounts of industrial and other wastes. Effective use of this approach typically involves reliance on the marketplace rather than regulatory action.

The role of the Illinois EPA in this arena is much less clearly defined than it is for the traditional regulatory programs. One pilot effort involves the Industrial Material Exchange Service initiated by the Illinois EPA and the State Chamber of Commerce in 1981. This Service is an information clearinghouse for industrial by-products, unused surpluses, off-specification materials and hazardous wastes.

The Service tries to enhance transfer opportunities between industrial facilities. In two years of operation, some 258 companies have submitted 379 material listings with the Exchange Service and the Agency has received over 1,000 inquiries about the Service. During this same period, companies reported total savings of over $860,000 and the recovery of over 7 million gallons of waste from use of the Service. On the basis of these results and expressions of support from participating companies, the Illinois EPA and the Chamber have elected to continue the Service.

The Illinois EPA has also encouraged the use of domestic wastewater treatment sludge for agricultural land, horticultural and silvicultural uses, for land reclamation projects and for public distribution. The Illinois EPA requires that sludges be adequately digested and applied such that safe application rates for heavy metals are not exceeded. In recent years, the practice of land application for domestic sludges has been gaining wider acceptance, and has become more widespread in Illinois. In recognition of the potential multimedia effects of sludge utilization, the Illinois EPA has prepared a special guidance document (December, 1982) which addresses all aspects of the Illinois EPA's sludge regulation activities.

ACHIEVING CLOSURE

Once the productive use of a chemical substance has passed, a means of handling it as a residual must be found. Some form of controlled release or disposal, such as emission to air, discharge to waterways or placement in or on the land, is usually chosen as the most practical mechanism. As has already been mentioned, the air and water pollution control and drinking water programs have a long history

of active management at the state level. Thus, refinement of the land pollution control program is necessary for "achieving closure" for the current environmental management system. This step is essential to complete the baseline of protection from which we can then launch the next round of effort for toxics control. The rest of this toxics strategy is based upon the assumption that the land pollution control program is fully operational.

Containment Of Wastes

Land pollution control requirements for disposal sites have traditionally been based upon the concept of "containment". In theory, substances placed in designed landfills are not expected to migrate outside the boundaries of the control structures to any significant degree over the short-term (decades). However, very recently, several situations in Illinois have raised concerns that certain liquids (organic solvents in particular) may move through clay barriers relatively quickly, often carrying other contaminants. Thus, as a reasonable precaution we concluded that further restrictions are appropriate for landfilling of liquid hazardous wastes in Illinois. Such restrictions are intended to maintain landfilling as more of a dry-materials technology in the future to minimize opportunities for release of contaminants underground. Many of these liquid wastes, particularly the solvents, are amenable to recycling and capacity for taking such action appears to be readily available.

State legislation passed in 1983 lays the groundwork for more rigorous control of liquid hazardous wastes and eventually all hazardous wastes. These actions, taken in concert with full implementation of federal requirements under the Resource Conservation and Recovery Act (RCRA), will all help "achieve closure"

on the current environmental management program in the very near future.

Dispersed Chemical Substances

Some types of business activities, such as agriculture and residential pest control, result in extensive dispersion of chemical substances. These activities demonstrate that often there is a fine line between when a substance is a resource and when it becomes a waste. Most of the regulatory control in this arena stems from the Federal Insecticide, Fungicide and Rodenticide Act, and the Illinois Pesticide Act. Under these Acts, the Illinois Department of Agriculture has the lead role for prevention and correction of problems stemming from improper control of these substances. The Illinois Pesticide Act establishes an Interagency Committee on Pesticides which, among other things, has the following mandate:

> Consider the problems arising from pesticide use with particular emphasis on the possible adverse effects on human health, livestock, crops, fish, and wildlife, business, industry, agriculture, or the general public.

The Illinois EPA recognizes the need to coordinate the implementation of a toxics control strategy with the Illinois Department of Agriculture. The Interagency Committee may eventually serve as a key vehicle in this process.

INTERACTION AMONG THE ENVIRONMENTAL PROGRAMS

With land disposal fast being foreclosed as a relatively inexpensive and convenient alternative to air and water discharges, we must begin looking at new ways to handle waste. This, in turn, will put pressure on the traditional pollution control programs for air and water. For example, the Illinois EPA expects waste incineration to increase substantially in the next five years. While this technology can be used safely, the current State regulatory program needs refinement in order to ensure that additional problems do not arise.

In the water program, studies show that toxic substances are more treatable than was assumed in the mid-70s. But just how treatable and at what cost is still being evaluated. Of course, treatment of these substances usually results in residual sludges that must still be managed properly. Control of these sludges oftentimes involves multimedia considerations as was mentioned previously.

Coping with environmental emergencies has served to highlight the gaps, overlaps, and disparities among the various environmental programs. Once the crisis atmosphere surrounding an episode has passed, the Illinois EPA is invariably faced with the problem for site remedial actions of "How clean is clean?" Comprehensive criteria are not readily available to assist staff with the development of site assessments and cleanup strategies. In the spring of 1983, the Agency began a pilot effort to develop cleanup criteria using case-by-case experience as evaluated by an internal technical panel.

The activities of the Coordinated Permit Review Committee established by the Illinois EPA about three years ago has also identified areas where media program interaction needs to be enhanced. Numerous cases have arisen where permit

applications which appeared satisfactory to one program would have, in fact, caused compliance problems for other programs. Over the past year, the Illinois EPA has enhanced tracking and reporting procedures in order to more effectively address some of these concerns, but we remain sensitive to the difficulties and complexities of preventing potential toxics problems from "slipping through the cracks".

Finally, careful review of the program information provided in Appendix A helps to point out the significant challenge we face in moving towards a more integrated approach to toxics control. Each major program has a complex legal, technical and procedural structure. These programs are essentially designed to operate in an independent manner and are driven by strong ties to specific federal program grants. The scope of their coverage of and the degree to which they control toxic substances is highly variable. Thus, at the state level we face the dual task of building better bridges among the environmental programs and also forging improved linkages with control programs such as TSCA.

DEVELOPMENT OF A STRATEGY

Basic Building Blocks

These developments are but a few highlights from among many events that have brought the Illinois EPA to address the need for an improved program for toxics control. Looking at these programs from a systems perspective, one key concern is the design of better performance standards for ensuring relatively safe emissions and discharges. This concern represents a step beyond and builds upon the recent federal regulatory focus upon technology-based control requirements. This problem needs to be addressed by focusing on the generic issue of how to regulate

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pollutants. A case can be made that the effort to shift from control of "conventional" (biochemical oxygen demand, total suspended solids, total particulates, etc.) to control of "toxic" pollutants has really been a matter of degree. Many of the pollutant parameters commonly called conventional also serve as composite, surrogate measures for the many unique substances contained in emissions and discharges. Thus, technological control efforts have already been addressing toxics in an indirect sense. But has this control effort been sufficient? Is toxicity being eliminated in the broadest sense? Answering these questions does not appear possible utilizing only chemical testing. Preventing toxic impacts from chemical substances implies use of biologic performance criteria as well. Thus, epidemiologic and environmental toxicity data appear to be necessary for meaningful assessment of relative risks posed by exposure to environmental contaminants, and eventual determination of acceptable performance standards. In fact, in many instances the use of biological monitoring procedures may prove to be the more cost-effective approach to regulation of complex mixtures of chemical substances.

Other important considerations for development of acceptable performance standards involve the degree of specificity and integration of their application. Environmental regulatory mechanisms have often been directed to generic specifications for controls. However, present demands appear to call for more site-specific prescriptions for targeted control programs. Such a shift in regulatory strategy brings forth questions of relative equity among facilities and certainty of protection for different publics. However, the current baseline of environmental protection certainly provides some measure of assurance in response to such questions.

Intuitively, there seems to be considerable merit to recognizing that not all facilities or chemical substances represent the same potential hazard under the multitude of possible environmental and exposure settings. Certainly from a business standpoint, affordability of control programs often, of necessity, relates to specific facilities as well. New corporate strategies for product stewardship could be brought into play with facility-specific assessments to fine-tune regulatory requirements. Illinois EPA monitoring activities need to follow suit as well. More and more, the public wants to know about all aspects of the facilities in their neighborhood and not about some abstract, statistical composite generated from a national standards program. Thus, more cooperative surveys and data sharing involving several state agencies will be needed to adequately define environmental problems and solutions.

A realistic toxics control strategy may also have to address a residual of uncertainty. This issue is hardly new to modern society. In many other public arenas, our culture has come to grips with the fact that total elimination of risk is not feasible. While there are laws to protect the public from auto accidents, crime, professional malpractice and other social phenomena, insurance is also used to cover the residual of uncertainty that is always present. The Illinois EPA must consider a broad range of risk management techniques as a reasonable hedge against technical uncertainty, undue economic hardship and proper concern for public safety. Environmental impairment liability insurance and financial assurances are already being utilized in the RCRA program and perhaps should be considered for a wider spectrum of environmental circumstances. These mechanisms may even be viewed as alternatives to the pursuit of "zero risk."

Finally, adopting a systems perspective implies looking beyond just the confines of the environmental regulatory programs. Pursuit of regulatory programs often involves certain opportunity costs that need to receive more careful attention as programs mature. The public demands and deserves adequate protection from improper use and control of chemical substances. But certainly the argument can be made that we have come a long way in recognizing and effectively coping with managing chemicals for the net benefit of society. Progressive regulation in the future must serve to build better bridges between social acceptability and practical constraints.

Decision-making Process

An inherent dilemma must be addressed in the development of a multimedia toxics control strategy. Since the media programs have developed along very independent paths, how, then, can one effectively address controlling toxics in the broadest sense without becoming mired down in the extensive framework of the current regulatory system? One answer is to simply set aside existing program requirements at the outset and focus instead on what should be achieved through a toxics control strategy. This was done by using a management by objectives (MBO) technique that included the following elements:

Program Goal — A short statement of the total result expected from the multimedia toxics control program. Related assumptions are provided to set the overall context within which the program operates.

Program Objectives — Short, results-oriented statements about the products necessary to achieve the program goal.

Action Plans — Specific activities necessary to achieve the stated objectives. Functional descriptions of both work items and schedules give these plans operating meaning.

We also recognized, however, that at some point this abstract MBO exercise would need to be interfaced with the realities and constraints of the existing regulatory programs. We chose to design this interface into the process between the program objectives and action plans phases. In other words, we set up the development of the program goal and objectives as an abstract "top down" exercise and the development of the action plans as a "bottoms up" exercise. In a very practical sense, this approach was an effort to fashion a compromise between the desire to achieve new direction and focus for toxics control and the requirements of the current regulatory structure.

The process began with the formation of a Toxics Project Team, made up of staff representing the full range of activities managed by the Illinois EPA (See Appendix B). This Team began operation in March, 1982 and spent the first six months conducting an intensive information sharing effort. In essence, we planned to develop a small core of technical staff who would eventually acquire special, expanded expertise in toxics control. In addition, we saw the need to supplement this team with a few highly specialized technical staff. This led to the creation and funding with state resources of the "Office of Chemical Safety" in 1983.

In order to address external communications, a Toxics Advisory Committee was also formed, made up of professionals from outside the Illinois EPA (See Appendix B). This Committee began operation in September, 1982 and also participated in special briefings on program activities and other information sharing in order to provide guidance early in the process before key aspects of the strategy were developed. In March, 1983, a joint session was held involving both the Project Team and the Advisory Committee.

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The actual MBO process was not initiated until May, 1983. At that time, a range of options for a proposed program goal was presented to the Advisory Committee for discussion. These options were developed from suggestions provided by Committee members and from approaches being considered by the Illinois EPA. In June, 1983, a first draft of proposed program objectives relating to the working concept for the program goal was presented to the Advisory Committee. At this point we reached a critical juncture where we needed to reinforce the dialogue on the toxics strategy with the Senior Managers in the Illinois EPA. Thus, in July, 1983, the Senior Managers held two special planning sessions to discuss the program goal and objectives. After these sessions, the program staff began to develop the specific action plans. We initially encouraged the program staff to carry forward as they saw fit in terms of achieving necessary interfacing of the MBO concepts and the actual operating programs. Finally, additional review and editing was conducted by the Project Team, the Senior Managers and the Advisory Committee during the fall of 1983.

TOXICS CONTROL STRATEGY

The results of the MBO process represent the toxics control strategy. The following program goal serves as the general statement of policy for guiding our efforts to ensure chemical safety in Illinois:

> Elimination of unreasonable risk of adverse effects on human health and the environment from exposure to toxic pollutants.

We view the achievement of this goal from a ten-year perspective. Such a timeframe is neither so short as to be over-optomistic nor so long as to be total speculation. This timeframe also conveys our belief that implementation of sound programs takes time, and that the current situation provides an opportunity for a phased approach to control of toxics.

This program goal is based upon the following assumptions which define the overall context within which we must operate:

- Risk has definable limits.
- Science and public policy-making are discrete processes.
- Quality of life considerations are relevant.
- Resources and technology available for risk reduction activities are limited.
- Implementation actions involve balancing of interests to achieve socially acceptable results.
- Funding support for regulatory programs will, at least, remain constant during strategy implementation.
- Legal authority may be essential for strategy implementation.

In order to realize the program goal, specific program objectives (See Appendix C) were established. These objectives set forth an orderly process for implementation of six major sets of activities as follows:

1. Existing legal authority and current programs should be focused more effectively for enhanced control of toxic pollutants. Priority attention should be given to the following areas:

   a. Facility compliance;
   b. Coordinated permit processing;
   c. Emergency response and cleanup;
   d. Coordinated interagency response to toxic hot spots;
   e. Non-regulatory initiatives and incentives;
   f. Limited enhancement and fine-tuning of operating programs; and
   g. Public participation and relations.

2. The Agency's new "Office of Chemical Safety" should be fully developed to ensure the adequacy of technical support and integration for toxics control.
3. A comprehensive problem assessment should be conducted by development of an adequate data base to characterize the nature, extent and impact of toxic pollutants.
4. Risk analysis and management practices should be selected and incorporated into the major environmental programs based upon an Agency-wide protocol.
5. New toxicity control requirements and risk management practices should be implemented to address defined problems in a timely manner.
6. The results of this program should be assessed to evaluate the adequacy of the process.

The detailed action plans, which were developed to specify the tasks and schedules necessary to achieve the objectives, are attached in Appendix C. While some plans are properly refined as of this date, many others need further attention over the next year to address various issues of multimedia coordination and priority setting. Formal project management techniques will be used to interrelate these materials in an accountable manner.

The products of the MBO process represent a concrete blueprint for moving forward on toxics control. We readily recognize that further refinement of the total resource implications of this strategy will be necessary over the next year in particular. Enough work has been done, however, to reach several general conclusions:

1. Some incremental progress can be achieved simply by redirecting resources that are currently available;
2. Certain fundamental activities, such as targeted data gathering and toxicity assessment, must proceed expeditiously in order to provide even a minimum basis for the control program;
3. Full scale integration and coordination of the toxics control effort is likely to be an iterative process, especially in view of the new information to be obtained and experience to be gained over the next few years; and
4. Continued pursuit of the aims of this strategy is necessary as an action-forcing mechanism to ensure full public disclosure of the need for adequate toxics control, and as a means of enhancing the consideration of trade-offs that are often necessary for actual program implementation.

CHEMICAL MANUFACTURERS ASSOCIATION

WILLIAM M. STOVER
Vice President
Government Relations

May 7, 1984

Honorable David Durenberger
Chairman, Subcommittee on Toxic
Substances and Environmental Oversight
United States Senate
Washington, D.C. 20510

Dear Senator Durenberger:

I have enclosed a statement which presents the Chemical Manufacturers Association (CMA) view of the National Research Council (NRC) report that was the subject of your subcommittee's hearing held on April 10, 1984. We appreciate your willingness to keep the record open for our statement.

The NRC study does have some relevance to regulatory practices, even though the study was not designed to evaluate the adequacy of toxicity data for use by the regulatory agencies. In particular, Part 2 of the NRC report emphasizes the need for expert judgment in making test decisions. Although only Part 1 of the report was the subject of the April 10 hearing, CMA urges that the complete report be evaluated to assess its relevance to current regulatory and voluntary testing activities.

CMA hopes that this statement will help the Senate gain a better understanding of the NRC report, and its relevance to EPA's regulatory practices. If you wish to discuss this statement, please have your staff call H. Christopher Nolde at 887-1134. Thank you for the opportunity to present this statement for the record of the April 10, 1984, hearing.

Sincerely,

wmstover

William M. Stover

WMS/ver

Formerly Manufacturing Chemists Association—Serving the Chemical Industry Since 1872.
2501 M Street, NW • Washington, DC 20037 • Telephone 202/887-1122 • Telex 89617 (CMA WSH)

CHEMICAL MANUFACTURERS ASSOCIATION

STATEMENT OF THE

CHEMICAL MANUFACTURERS ASSOCIATION

TO THE

SUBCOMMITTEE ON TOXIC SUBSTANCES AND ENVIRONMENTAL OVERSIGHT

U.S. SENATE

HEARING ON NATIONAL RESEARCH COUNCIL

REPORT TOXICITY TESTING: STRATEGIES TO

DETERMINE NEEDS AND PRIORITIES

APRIL 10, 1984

May 7, 1984

2501 M Street, NW • Washington, DC 20037 • Telephone 202/887-1100 • Telex 89617 (CMA WSH)

EXECUTIVE SUMMARY

The National Research Council (NRC) recently published the results of a study on toxicity testing sponsored by the National Toxicology Program (NTP). The NRC study was designed to respond to the following assignments: 1) Estimate the amount of readily available toxicity data as an indication of potential testing needs for federal health agencies; and 2) Develop a priority-setting mechanism for selecting chemicals for testing. Part 1 and Part 2 of the NRC report address these objectives in order.

Part 1 of the NRC study must be evaluated within the limits imposed by its design. Part 1 estimates the amount of toxicity test data published in readily available files. Unpublished results, recently completed tests, or confidential data were not included. Furthermore, the substances selected for in-depth review were chosen at random, and not on the basis of toxicity or exposure, the very factors that Part 2 of the study requires to determine the need for further toxicity testing. Thus, Part 1 of the NRC study does not estimate testing needs for regulatory programs focused on chemicals of higher potential concern.

CMA member companies have long recognized the need for further toxicity testing of such commercial chemicals of concern. Many of the member companies of CMA have voluntarily sponsored individual and collective efforts to produce toxicity data necessary for risk assessment of priority chemicals of potential concern. Congress also recognized the need for priority-setting in toxicity testing when it passed the Toxic Substances Control Act (TSCA) in 1976. Under TSCA, the Interagency Testing Committee (ITC) has developed, applied, and refined a priority-setting mechanism that is similar, but more precise, than the mechanism recommended in the NRC report.

Although toxicity tests are performed for the immediate purpose of evaluating toxicological effects, the ultimate purpose is risk assessment, which requires consideration of both toxicity and exposure. Evaluating the interplay between these factors requires considerable expertise and judgment. In assessing risks and making test decisions, neither toxicity nor exposure can be evaluated independently. These considerations require case-by-case analysis on the basis of expert judgment. Indeed, the NRC study itself concludes, "Testing priorities have traditionally been assigned on the basis of expert judgment... The committee believes that this basic pattern should continue, with further improvement in techniques that allow expert judgment to be most effective."[1]

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[1] NRC Report, p. 205.

1. INTRODUCTION

This statement reflects the Chemical Manufacturers Association (CMA) view of the NRC report, Toxicity Testing Strategies to Determine Needs and Priorities,[2] that was the subject of a hearing held by the Senate Subcommittee on Toxic Substances and Environmental Oversight on April 10, 1984. While the hearing covered only Part 1 of the NRC report, Part 2 of the study should also be reviewed because its findings are relevant to policy decisions regarding the need for increased toxicity testing. Although CMA recognizes the need for further toxicity testing of commercial chemicals of higher potential concern, Part 1 of the NRC study does not evaluate toxicity testing needs in this way. By design the NRC study answers only certain questions and the conclusions that can be drawn are limited because of testing activities and factors that the NRC study did not include.

The NRC study reviewed only readily available toxicity data, and thus did not consider the results of unpublished or recently completed testing. These testing activities include not only the individual efforts of CMA member companies, but also the pioneering research performed at the Chemical Industry Institute of Toxicology (CIIT). In addition, CMA facilitates individual and collective testing programs sponsored by chemical companies in response to the testing

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[2] National Academy Press, Washington, DC. (1984). The study referred to was titled "Identification of Toxic and Potentially Toxic Chemicals for Consideration by the National Toxicology Program". Hereinafter, the study and report will be referred to simply as the "NRC study" or the "NRC report".

recommendations of the Interagency Testing Committee (ITC). Section 2 of this statement presents an overview of the recently completed and ongoing testing activities that were not included in the NRC study.

As explained in Section 3 of this statement, the NRC study was designed to estimate the amount of readily available toxicity test data and to develop a priority setting mechanism for the selection of chemicals for testing. The report's findings must be interpreted with these limits in mind. The NRC itself clearly states this point: "The review reported herein was not undertaken as an 'audit' of the adequacy of past regulatory policies or procedures, and the data developed in this study are not likely to be immediately useful for regulatory purposes."[3]

The regulatory agencies need toxicity test data for risk assessment, a complex scientific assessment which requires consideration of exposure information. In a separate report, the NRC defined risk assessment as "the use of the factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations."[4] In that report, the NRC identifies four steps to obtain a risk assessment:

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[3]NRC report, page 75

[4]Risk Assessment in the Federal Government: Managing the Process. National Academy Press. Washington, DC. 1983.

- Hazard identification
- Dose-response assessment
- Exposure assessment
- Risk characterization

Toxicity testing usually addresses the first two steps. Since characterization of risk requires consideration of the extent of human exposure, however, a determination of the need for toxicity testing of a substance must also consider the potential for human exposure.

Since toxicity tests are ultimately used for risk assessment, controls which confine a substance to low potential exposure, and thus minimize risk, can obviate the need for extensive testing. Extensive testing of a substance with low human exposure would divert resources from higher priority testing where data are needed for risk assessment. For this reason, both government and private company researchers use priority systems to select chemicals for testing.

Section 4 of this statement compares the priority setting mechanism developed in part 2 of the NRC report with the priority setting mechanism applied by the ITC. Both the NRC and ITC systems use available information and expert judgement to screen chemicals for testing based on exposure and toxicological effects. Both systems also rely heavily on the input of scientific judgment to answer the complex questions in risk assessment that arise because of the interaction between exposure and toxicological effect. In discussing the evaluation of toxicity data for predicting human health hazards, the NRC report

concludes that "... expert judgment to insure the proper use of all available data is an essential part of each analysis."[5]

With regard to testing under Section 4 of TSCA, the later stages of the system developed by the NRC correspond to the stage in the ITC process where the ITC completes its review and recommends the chemical to EPA for more in-depth study. At this stage, EPA uses its authority under TSCA Section 8 (a) to require production, exposure, and use information. In addition, EPA uses its authority under TSCA Section 8(d) to require manufacturers and processors to submit all unpublished health and safety studies. Thus, once the ITC recommends a chemical to EPA, the Agency uses its TSCA authority to require submission of the information that the NRC found so difficult to obtain in Part 1 of their study.

In Section 5 of this statement, CMA outlines the role of the National Toxicology Program given the extensive testing programs of other government and private groups and the NTP's need for further information in order to establish priority in its testing program. The NTP should be a cooperative research effort which performs toxicity tests that further the following goals:

1) Basic research to develop a mechanistic understanding of toxicity and how this relates to the low doses of chemicals detected with ultrasensitive analytical techniques.

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[5]NRC report, page 65

2) Methods development to validate scientific techniques that can be used to accurately assess the potential human health effects of chemicals.

3) Testing and evaluation of natural carcinogens, environmentally generated chemicals, and chemicals not tested elsewhere.

To the extent that the NTP needs more information for its testing program, it should search the files of other agencies before requesting information from industry.

In Section 6 of the statement, CMA underscores two public policy conclusions that emerge from the NRC study. First, expert judgment on each case is a vital element of any system to determine the need for toxicity testing. Second, the ITC uses a sound procedure for recommending to EPA those chemicals that should receive high priority for toxicity testing under TSCA.

2. OTHER EFFORTS TO GENERATE TOXICITY DATA

The extent of toxicity testing needs depends in part, of course, on the amount of information already available. Part 1 of the NRC study did not review the results of unpublished or recently completed testing because of the limits of the information gathering process. The NRC report recognizes this limitation when it points out that "...some of the data bases failed to include the most recent research."[6] The NRC report also points out that unpublished or confidential data were in most cases not reviewed: "Evaluations...were based largely on published data or other publicly available information...".[7] As an example of these limitations, Part 1 of the NRC study did not review the results of recently completed tests that industry performed in response to the recommendations of the ITC. CMA member companies and other chemical companies have negotiated testing agreements with EPA that have, in 1983 alone, generated results from nearly 200 tests. These agreements will continue to generate toxicity data in the next few years.

While the TSCA mandated activities of the ITC and EPA have affected the chemical industry's toxicology testing activities, it should not be inferred that these efforts represent the totality of testing sponsored by chemical companies. Recognizing the need for data as well as the need for development of the scientific understanding of toxicology, the Chemical Industry

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[6] NRC report, page 72

[7] NRC report, page 72

Institute for Toxicology was established in 1978. CIIT maintains an active program for the generation of data on chemicals of widespread use. The institute is also engaged in research directed at elucidating toxicological mechanisms and extending this area of science. The annual budget for CIIT is nearly 10 million dollars.

Greatest of all testing activities is the research sponsored by individual companies. CMA undertook a survey of the toxicology testing facilities and activities of its member companies. In 1981, the 82 companies responding to the survey tested over 4,400 chemical substances. This testing required a significant expenditure of funds and a substantial investment in physical facilities. The 1981 cost to these companies of the testing was $138 million; the 1981 replacement value of the testing facilities was $255 million.[8]

In addition to these testing efforts for commercial chemicals, companies conduct or sponsor extensive testing of substances under development for use as drugs, pesticides and food additives. These efforts increase the understanding of toxicological effects and are thus useful for the evaluation of commercial chemicals.

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[8] An Industry Survey of Chemical Company Activities to Reduce Unreasonable Risk, Peat, Marwick, Mitchell and Company, Washington, DC (1983), page 22

3. TESTING NEEDS

Part 1 of the NRC study, Toxicity-testing Needs in the Select Universe, reports the results of two efforts:

1. Identification of the data needed to adequately characterize the potential hazard of a substance, and

2. Matching of these identified data needs with the data available for a sample of substances to assess the adequacy of the existing toxicological data base.

With regard to the data for hazard characterization, the NRC identified those data elements which it felt were needed for each different category of substances. Thus, the study differentiated between food additives, drugs, pesticides, and commercial chemicals, an appropriate and necessary distinction given the significant differences in use and exposure. The CMA will restrict its discussion in this document to commercial chemicals only.

The tests identified by the NRC for commercial chemicals[9] will more than adequately characterize the toxicological effects of these materials. This list, however, is so extensive that to generate the complete set of tests for just one substance would require a commitment of several years and millions of dollars. While the testing suggested would completely characterize the

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[9] NRC report p. 161-2.

toxicity of a commercial chemical, such extensive efforts are not always needed.

In developing testing programs for a given substance, there are a number of factors which a toxicologist must consider. A testing program is usually designed on the basis of existing data, intended end-use of the chemicals, and the likelihood and level of human exposure. In concert, these characteristics will dictate the responsible allocation of time and resources for necessary and sufficient toxicity testing. Thus, for valid reasons, all the tests identified by the NRC are not done for most commercial chemicals.

Since toxicity testing programs are logically based on hazard and potential for exposure, it is not surprising that Part 1 of the report concludes that there is a paucity of toxicological data for commercial chemicals. The analysis of data needs was conducted without consideration of use and exposure patterns and therefore is an evaluation of hazard assessment only. The NRC explicitly adopted an approach that, "required judgements on the adequacy of testing of specific substances, independently of whether the substances were potential agents or relatively inert substances with low toxicity."[10]

The assessment of risk posed by commerical chemicals will require varying amounts of toxicity data depending on the magnitude of the potential exposure to a substance. The toxicity data required for risk assessment must be determined on a case-by-case basis, not by meeting the requirements of a checklist.

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[10] Ibid., p. ix, (emphasis added).

4. SETTING PRIORITIES

The demand for toxicity data, and consequently the need for priority in toxicity testing, has grown with the increased use of chemicals in our society and the development of more definitive toxicology tests, as well as with the ability to detect the presence of substances at extremely low concentrations. Partly in response to these data demands, Congress included certain testing requirements in section 4 of the Toxic Substances Control Act (TSCA). At about the same time, industry organized the Chemical Industry Institute of Toxicology to conduct independent testing and research. Furthermore, individual companies built or expanded in-house toxicology testing facilities, and have also banded together in joint testing programs under the auspices of CMA and other organizations. Because of time and resource limitations, all of these programs need to establish priorities to maximize the benefit of testing efforts.

Part 2 of the NRC report recommends a priority setting mechanism which is very similar to the approach being used by the Interagency Testing Committee (ITC), which Congress established in Section 4(e) of TSCA. The ITC consists of representatives of a number of federal government departments and agencies.

Since its formation in April 1977, the ITC has been reviewing industrial chemicals and recommending testing on those chemicals which it concludes may adversely affect man or the environment and for which adequate data are lacking. The recommendations are made to the EPA, which, if it concurs, can formally require industry to carry out the tests under Section 4 of TSCA.

Over the years, the priority/selection/scoring system that the ITC uses has evolved from that first published by Nisbet[11] and reviewed by the NRC.[12] Today the ITC selection system is an effective, efficient system which contains the elements suggested in Part 2 of the NRC Report and, in some areas, goes beyond the NRC recommendations.

Both systems screen large numbers of chemicals, and then set priorities to pare them down to a manageable number. Exposure and toxicity assessments are central to test selection in each scheme. In the exposure area, production volume, occupational and general public use, are considered by both; but, in addition, the ITC also looks at potential for environmental release. Similarities also exist in the toxicity area. Although the NRC system is applicable to any toxic effect, it looks only at cancer, while the ITC is required by law to look at other effects such as mutagenicity, reproductive effects, acute toxicity, environmental factors, and ecological effects, with emphasis on the first three.

Both systems use readily available data sources, but in addition, the ITC asks for and receives voluntary submissions of data from the public and industrial sectors. Expert judgment is used extensively in both systems. The NRC approach, however, is somewhat more formal and possibly rigid in its use of that judgment.

Both systems only call for testing to eliminate uncertainty where adverse effects are anticipated. Where relative certainty exists about the hazard, either positive or negative, no testing is recommended in either system. Table I provides a generalized comparison of the two approaches.

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[11]Nisbet, I.T.C., 1979, Ranking chemicals for testing: A priority-setting exercise under the Toxic Substances Control Act, pp. B-41 to B-54. In Scoring Chemicals for Health and Ecological Effects Testing. TSCA-ITC Workshop. Rockville, MD, Enviro Control, Inc.

[12]NRC report, pp. 310-312.

TABLE I

GENERAL COMPARISON OF ITC AND NRC PRIORITIZATION APPROACHES

ITC	NRC STAGE I AND II
TSCA Inventory	Universe of Chemicals
Volume Produced	
Preliminary Screening	
- Previously Scored	
- Already Regulated	
- Well Understood	
- Poorly Characterized	
Exposure Scoring by Experts	
- Annual Production	- Production Volume
- Fraction Released	- Use Class
- Persistence	- Expert Judgement
- Number of People Exposed	- Micro-Dossier
- Frequency of Exposure	
- Intensity of Exposure	
- Penetrability	
- Number of Workers Exposed	
Biological Scoring by Experts	
- Automated Information SANSS, RTECS, etc.	- Toxic Effects Reported (RTECS)
	- Toxic Class (SAR/SANSS)
- Expert Judgement	- Expert Judgement
-- Health Effect, Cancer, Muta, Repro, etc.	- Micro-Dossier
-- Environmental Factors	
Preliminary Draft Review	- Mini Dossier

In-Depth Review

- Exhaustive Computer & Manual Search of Liter.
- Direct Request to Mfg. for Unpublished Information
- Formal Document of Findings
- Expert/Committee Review
- Recommend Testing to EPA

EPA Review

EPA Recommendation for Section 4 Test or Voluntary Test Agreement

NRC Stage III

- Primary; Secondary & Computer Liter. Search
- Dossier Preparation
- Expert Review

NTP Scientific & Policy Review

NRC Stage IV

- Testing

The TSCA Inventory of Existing Chemicals has been available since the Third ITC Scoring Exercises in 1980. In subsequent scoring exercises, the ITC has utilized the TSCA Inventory as a starting point, but has supplemented it with additional bases. Moreover, beginning with the Fifth Scoring Exercise, the ITC has has access to the confidential inventory and to all confidential information submitted by companies to EPA on the ITC.

Once the initial group of chemicals for review is selected, a Preliminary Screening is carried out. Materials that have been previously scored, already regulated (ITC only has responsibility for TSCA chemicals), well understood toxicity (e.g., vinyl chloride monomer or water), and poorly characterized mixtures are eliminated. This preliminary screening is carried out partially by computer and partially by the exercise of expert judgment (a team made up of a toxicologist, medicinal chemist, biochemist and environmental chemist).

Once the Preliminary Screening is completed, the chemicals that remain (598 in the Third scoring exercise; 413 in the Fourth exercise; 510 in the Fifth exercise) are subjected to an extensive exposure scoring.

As with the NRC approach, the ITC uses several experts to evaluate exposure (environmental chemist, chemical engineer, industrial hygienist and exposure specialist). The experts develop four different exposure indices. When specific data are not available, judgments are used, and scoring is based on experience with similar chemicals, uses, and processes. When scorers are in doubt, they lean towards assignment of high scores. This approach biases the scoring towards high exposure but tends to minimize false

negatives. In theory, only those chemicals with high exposures are retained for the biological/toxicological scoring. In practice, however, a material can be retained if in the opinion of the experts it has low exposure and possible significant biological activity.

At this point, those chemicals which have passed through the exposure scoring screen undergo biological scoring (toxicological evaluation). As with the NRC approach, automated information bases such as SANSS, RTECS, Toxline, Medline, Enviroline, etc., are used as well as information on physical and chemical properties to generate information profiles (micro dossier) for use by the biological experts.

In the ITC system, four panels of experts use these profiles to assign scores for eight biological factors: Mutagenicity, carcinogenicity, teratogenicity, reproductive effects, acute toxicity, other toxic effects, bioaccumulation, and ecological effects. Those materials which are judged to posses possibly high biological activity and for which toxicity data are inadequate, are retained for further evaluation.

At this point in the screening process (end of NRC Stage 2; completion of ITC Biological Scoring) both systems recommend that a detailed review be carried out on those chemicals which remain. (Table II shows the number of chemicals that have been retained at each step of the screening for the Third, Fourth and Fifth ITC reviews.) The ITC has arrived at this point by use of available data and confidential business information, sequential exposure and toxicity assessments and expert judgments. The NRC approach

s available data, concurrent exposure and toxicology assessments, expert gments and somewhat heavier reliance on formalized decision rules.

For materials that have reached either Stage 3 (NRC) or In-Depth Review C), exhaustive computerized and manual searches of the published litera- re are carried out in both approaches. Unfortunately, not all the avail- le information is contained in the published literature. In general, chnical journals do not publish studies which show no adverse effect.

TABLE II

CHEMICALS REVIEWED IN ITC's SCORING EXERCISES

	3rd Exercise	4th Exercise	5th Exercise
	TSCA Inventory		
Initial List	1,877	2,752	2,921
Preliminary Screening	598	413	510
Exposure Scoring	207	218	214
Biological Scoring	107	79	82
	Chemicals Selected for In-Depth Review		

Considering this, and realizing that it would be in everyone's interest to have access to any additional data (toxicity, exposure, use, etc.) that could be made available, the ITC publishes requests for the voluntary submission of data.[13,14] EPA has indicated that the response to these requests has been excellent. This approach to obtaining access to available unpublished data is not a part of the NRC system and might be a worthwhile addition.

In the ITC approach, a testing recommendation is made to EPA which then has twelve months to decide whether the recommended testing is needed. To make that decision, EPA invokes its authority under Section 8 of TSCA which requires manufacturers and processors to provide any information they may have on toxicological effects (health and safety studies) as well as information on production volume, uses, and exposure. Once EPA has evaluated all the available information, it may require testing if it deems it necessary.

Both the NRC and ITC approaches appear to be reasonable methods of selecting those industrial chemicals which require testing, and the types of tests required. Since both systems evaluate the same type of data in somewhat the same manner, the final results should be substantially the same.

The ITC, with its scoring approach, supplemented by the increased access to unpublished and confidential information that has been developed in recent years, is handling the need for identifying those industrial chemicals that may need additional testing.

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[13] Federal Register 45, 66506, October 7, 1980.

[14] Federal Register 47, 8244, February 25, 1980.

5. THE ROLE OF THE NTP

The increased testing activity on TSCA chemicals described above suggests that the National Toxicology Program should not primarily concern itself with the testing of those chemicals which fall within the purview of TSCA. A mechanism exists and is functioning for the identification of TSCA testing needs and the implementation of programs to meet these needs.

The efforts of the NTP should supplement, rather than duplicate, the above-described efforts. To this end, we believe NTP should direct its program towards the following areas:

1) Basic research to develop a mechanistic understanding of toxicity and how this relates to the low doses of chemicals detected with ultrasensitive analytical techniques;

2) Methods development to validate scientific techniques that can be used to accurately assess the potential human health effects of chemicals; and,

3) Testing and evaluation of natural carcinogens, environmentally generated chemicals, and chemicals not tested elsewhere.

To the extent that the NTP needs more information for its testing program, it should first tap the files of other agencies before requesting redundant information generation and submission from industry.

6. PUBLIC POLICY CONCLUSIONS

Although the NRC report does not comment directly on issues of public policy with respect to toxicity testing, the report nevertheless states or leads to some important policy conclusions.

1) Assessment of the need for toxicity information on a specific substance depends on the application of expert judgement to each situation rather than on rote application of general standards.

Whether the need is defined in the abstract scientific sense used in the first part of the report or in the concrete context of priority-setting, the need for information on a particular substance cannot be identified solely by comparing the available information to pre-determined sets of toxicity data "requirements." Rather, as Part 1 of the NRC report repeatedly underscores, "expert judgement to insure the proper use of all available data is an essential part of each analysis"[15]. The second part of the report reaffirms the same principle: "Testing priorities have traditionally been assigned on the basis of expert judgement. . . The committee believes that this basic pattern should continue, with further improvement in techniques that allow expert judgement to be most effective."[16]

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[15] NRC Report, p. 65.

[16] NRC Report, p. 205.

2) The ITC has followed a well-designed priority-setting mechanism to bring to EPA's attention those chemicals for which further testing may be appropriate.

The close similarity between the ITC scoring system and the model mechanism that the NRC committee developed confirms the fundamental soundness of the ITC procedure in guiding EPA's testing program under the Toxic Substances Control Act. This does not mean that every chemical substance the ITC nominates must be tested. From time to time, closer evaluation of a designated substance by EPA, or the production of new exposure or toxicity information from industry sources or through recent testing, will answer the testing needs that led the ITC to designate the substance. The ITC's review process, however, clearly follows the recommendations of the NRC report.

NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION
THE MADISON BUILDING
1155 Fifteenth Street, N.W., Washington, D. C. 20005
202 • 296-1585 Cable: NAGRCHEM

Dr. Earl C. Spurrier
Vice President
Regulatory Affairs

April 30, 1984

The Honorable David F. Durenberger
Chairman
Subcommittee on Toxic Substances and
Environmental Oversight
U.S. Senate
Washington, D. C. 20510

Re: Hearing on Toxicity Testing of Chemicals
April 10, 1984

Dear Chairman Durenberger:

The National Agricultural Chemicals Association* wishes to submit the following comments for the record concerning the report entitled "Toxicity Testing - Strategies to Determine Needs and Priorities" (Report) which was released on February 28, 1984 by the National Research Council of the National Academy of Sciences

NACA has no difficulty with the intent of the study to determine the priorities for testing chemicals which may cause human health hazards. However, we believe that the Report does a disservice to the regulated industries and to the reputation of the Academy as its sponsor. For the reasons stated, NACA disagrees with the conclusion that toxicity information is lacking for 38 percent of pesticides which are registered with the Environmental Protection Agency (EPA).

Although the Report carefully mentions several disclaimers about the way in which the authors reached their results without having total access to the information about each chemical, it appears to us that the authors should have made more allowance for this deficiency, and should have even

*The National Agricultural Chemicals Association (NACA) is a nonprofit, trade organization of manufacturers and formulators of pest control products employed in agricultural production. NACA's membership is composed of the companies which produce and sell virtually all of the technical crop protection materials (active ingredients) and a large percentage of the formulated products registered for use in the United States.

excluded certain classes of chemicals from their study. To do otherwise, the authors ignored significant facts to reach their conclusions. These omissions diminished the recommendations in the Report for more toxicity testing, and leave the wrongful impression that the public is not being adequately protected by statutes and regulations already in place.

In regard to pesticides, the Report (1) ignores the definition of an active ingredient in a formulation; (2) ignores data which are available to federal agencies for inspection and evaluation; and (3) ignores other factors such as exposure data which generally show chemicals to be relatively safe.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) requires a full spectrum of toxicology and environmental data before the uses of any pesticide can be registered and marketed. Under FIFRA regulations established by the EPA, protocols for testing have been developed to guide registrants to submit extensive data to the Agency. The data must be developed for all "active ingredients" which are generally defined as the ingredients in a pesticide formulation which will "prevent, destroy, repel or mitigate any pest." These tests are not necessarily required for "inert ingredients" which are the other chemicals in the formulation which are not "active." The inclusion of pesticides and inert ingredients into one category distorts the picture regarding the existence or lack of testing data available.

Therefore, the data on all active ingredients (and many inert ingredients) have been submitted to EPA and evaluated by that Agency. The authors could have determined this fact by merely reviewing the Registration Guidelines and regulations which are available to the general public.

When EPA evaluates the data submitted by registrants, it uses a risk-benefit criteria which are based in part on the probability of exposure and attendant risk as a result of that exposure. The NAS Report fails to take this factor into account, but chooses instead to only consider the risks. On that basis, there would be many products which would not be registered, even though the risk of exposure to the harmful effects of a chemical would be miniscule.

The authors have established their own criteria for adequacy of data, which are different from the criteria established by FIFRA or the Food, Drug and Cosmetic Act (FDCA). The EPA employs the criteria of these two laws to make a safety evaluation, and approves the labels which are placed on products before they can be marketed to the general public. It is regretful that the National Academy of Sciences has superimposed itself on this regulatory process.

Finally, and more importantly to our industry, further damage to the reputation of pesticides was done by the press release from the National Research Council. That document distorts the document it purports to summarize, and fails to acknowledge the disclaimers which recognized the deficiencies in the approach taken by the Report. In fact, in testimony before the your Subcommittee on April 10, 1984, the authors admitted that the availability of additional data would change the results of the Report and improve the conclusion about the adequacy of testing. We submit that the authors could have had information whether data exists if they had only checked the pesticide regulations.

In summary, the National Research Council should have excluded agricultural chemicals which already have toxicological profiles as required under law, and should have recognized the existence of required data, albeit confidential information, in the EPA files. Having failed on both points, the Report does not support any meaningful conclusions about agricultural chemicals, or any chemicals in the same regulated posture.

Very truly yours,

Earl C. Spurrier

Earl C. Spurrier

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